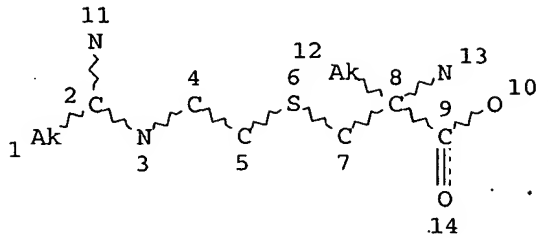
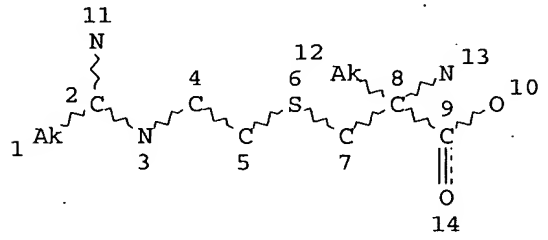
```
=> d que stat l7
L5                STR
```

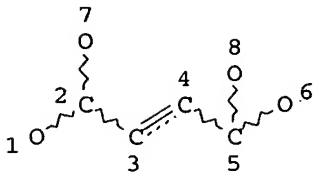



```
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E1  RC AT  10
CONNECT IS E1  RC AT  11
CONNECT IS E1  RC AT  12
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L7          163 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED    1743 ITERATIONS                 163 ANSWERS
SEARCH TIME: 00.00.01


=> d que stat l11
L5                STR
```




```
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E1  RC AT  10
CONNECT IS E1  RC AT  11
CONNECT IS E1  RC AT  12
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L7          163 SEA FILE=REGISTRY SSS FUL L5
```

L8 STR



NODE ATTRIBUTES:
CONNECT IS E1 RC AT 1
CONNECT IS E1 RC AT 6
CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 8
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
L11 4 SEA FILE=REGISTRY SUB=L7 SSS FUL L8

100.0% PROCESSED 24 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

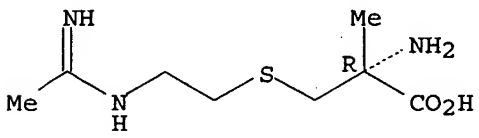
=> d ide l11 1-4
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

L11 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 753491-31-5 REGISTRY
ED Entered STN: 29 Sep 2004
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, hydrochloride, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C8 H17 N3 O2 S . x C4 H4 O4 . x Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

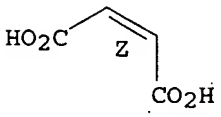
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

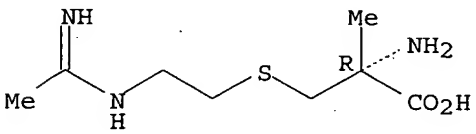
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 753480-15-8 REGISTRY
ED Entered STN: 29 Sep 2004
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C8 H17 N3 O2 S . x C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

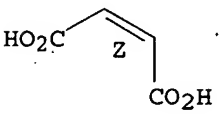
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

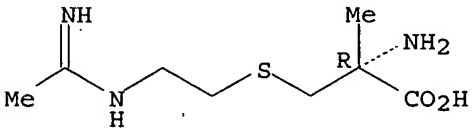
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 364068-09-7 REGISTRY
ED Entered STN: 23 Oct 2001
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C8 H17 N3 O2 S . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

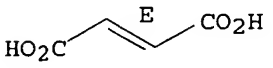
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



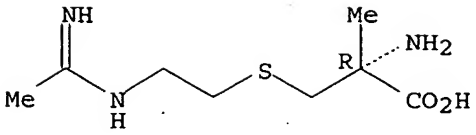
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 364067-80-1 REGISTRY
ED Entered STN: 23 Oct 2001
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C8 H17 N3 O2 S . 1/2 C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

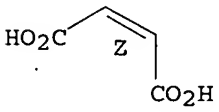
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

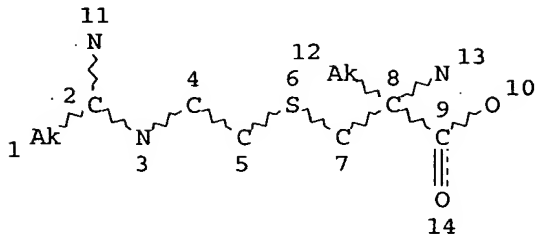


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

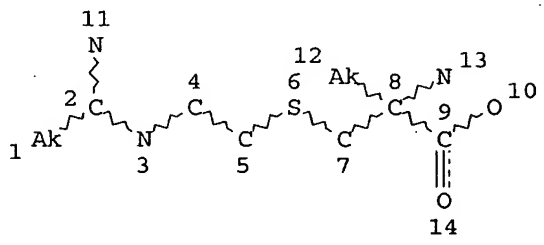
=> file stnguide
FILE 'STNGUIDE' ENTERED AT 08:39:46 ON 24 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 19, 2006 (20060519/UP).

```
=> => d que stat l14
L5                STR
```

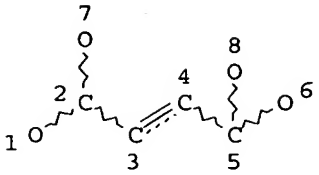



```
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E1  RC AT  10
CONNECT IS E1  RC AT  11
CONNECT IS E1  RC AT  12
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L14           0 SEA FILE=BEILSTEIN SSS FUL L5

100.0% PROCESSED     143 ITERATIONS                    0 ANSWERS
SEARCH TIME: 00.00.02


=> d que stat l36
L5                STR
```




```
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E1  RC AT  10
CONNECT IS E1  RC AT  11
CONNECT IS E1  RC AT  12
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L7          163 SEA FILE=REGISTRY SSS FUL L5
```

L8 STR

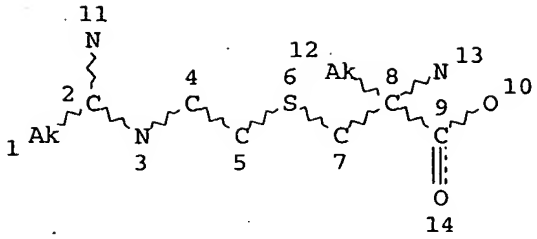


NODE ATTRIBUTES:
CONNECT IS E1 RC AT 1
CONNECT IS E1 RC AT 6
CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 8
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE

```
L11            4 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L17              QUE  ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY
                 <2004 OR REVIEW/DT
L18              QUE  ABB=ON  PLU=ON  ?CRYST?
L19              QUE  ABB=ON  PLU=ON  MELT? OR MP OR (M(W)P)
L20              QUE  ABB=ON  PLU=ON  (WATER OR H2O OR MOISTURE)(4A)(?SORB
                 ? OR ?SORP? OR ABSORB? OR ABSORP?)
L21              QUE  ABB=ON  PLU=ON  ?SOLUBIL? OR ?SOLUBL?
L22              QUE  ABB=ON  PLU=ON  XRAY OR (X(W)RAY) OR DIFFRAC? OR (PO
                 WDER(2A)PATTERN)
L23              QUE  ABB=ON  PLU=ON  RAMAN
L24              QUE  ABB=ON  PLU=ON  ?ANALY?
L25              QUE  ABB=ON  PLU=ON  TGA OR THERMAL? OR THERMO? OR DSC OR
                  CALORIM?
L33            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L34            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND (L18 OR L19 OR L20 OR
                 L21 OR L22 OR L23 OR L24 OR L25)
L35            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 OR L34
L36            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 AND L17


=> d his l40

     (FILE 'USPATFULL, USPAT2' ENTERED AT 08:53:30 ON 24 MAY 2006)
L40           11 S L39 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d que nos l40
L5               STR
L7             163 SEA FILE=REGISTRY SSS FUL L5
L8               STR
L11              4 SEA FILE=REGISTRY SUB=L7 SSS FUL L8
L39             11 SEA L11
L40             11 SEA L39 AND (AY<2004 OR PY<2004 OR PRY<2004)


=> d que stat l47
L5               STR
```



```
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E1  RC AT  10
CONNECT IS E1  RC AT  11
CONNECT IS E1  RC AT  12
CONNECT IS E1  RC AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L47          34 SEA FILE=WPIX SSS FUL L5

100.0% PROCESSED     165 ITERATIONS                          34 ANSWERS
SEARCH TIME: 00.00.04


=> d his l47-l60

     (FILE 'WPIX' ENTERED AT 08:59:24 ON 24 MAY 2006)
L47          34 S L5 FUL
                SAVE TEMP L47 VAL348WPIPS/A
L48          14 S L47/DCR
                SELECT L48 1- DCN
                SELECT L47 1- SDCN
L49          14 S E223-E256/DCN
L50          14 S L48 OR L49
L51          14 S L50 AND (L18/BIX OR L19/BIX OR L20/BIX OR L21/BIX OR L22/BIX
L52          14 S L50 OR L51
L53          14 S L52 AND (AY<2004 OR PY<2004 OR PRY<2004)
                SAVE TEMP L53 VAL348WPI1B VAL348WPI1B/A
L54           0 S L53 NOT L52
L55           0 S L52 NOT L53
L56          10 S L53 NOT L45
L57           6 S L53 AND L27/BIX
L58           0 S L53 AND ?BUTENOATE?
L59           0 S L53 AND ?BUTENOATE?/BIX
L60          14 S L53 OR L57-L59

=> d que nos l60
L5               STR
L47          34 SEA FILE=WPIX SSS FUL L5
L48          14 SEA FILE=WPIX ABB=ON  PLU=ON  L47/DCR
L49          14 SEA FILE=WPIX ABB=ON  PLU=ON  (RACSJE/DCN OR RACSJG/DCN OR
                RACSJJ/DCN OR RACSJL/DCN OR RACSJU/DCN OR RACSJW/DCN OR
```

```
                RACSJY/DCN OR RAFIL7/DCN OR RAFI3K/DCN OR RAFI4G/DCN OR
                RAFI57/DCN OR RAHF7P/DCN OR RAHF7Q/DCN OR RAHF7S/DCN OR
                RAHF7T/DCN OR RAHF7V/DCN OR RA5HUE/DCN OR RA5HUF/DCN OR
                RA5R8T/DCN OR RA5R8W/DCN OR RA5R8X/DCN OR RA5R8Y/DCN OR
                RA5R8Z/DCN OR RA5R9A/DCN OR RA5R9C/DCN OR RA5R9G/DCN OR
                RA5R9H/DCN OR RA5R91/DCN OR RA5R92/DCN OR RA5R93/DCN OR
                RA5R96/DCN OR RA5R97/DCN OR RA5R98/DCN OR RA5R99/DCN)
L50          14 SEA FILE=WPIX ABB=ON  PLU=ON  L48 OR L49
L51          14 SEA FILE=WPIX ABB=ON  PLU=ON  L50 AND ((?CRYST?/BIX) OR
                (MELT?/BIX OR MP/BIX OR (M/BIX(W)P/BIX)) OR ((WATER/BIX OR
                H2O/BIX OR MOISTURE/BIX)(4A)(?SORB?/BIX OR ?SORP?/BIX OR
                ABSORB?/BIX OR ABSORP?/BIX)) OR (?SOLUBIL?/BIX OR ?SOLUBL?/BIX)
                 OR (XRAY/BIX OR (X/BIX(W)RAY/BIX) OR DIFFRAC?/BIX OR (POWDER/B
                IX(2A)PATTERN/BIX)) OR (RAMAN/BIX) OR (?ANALY?/BIX) OR
                (TGA/BIX OR THERMAL?/BIX OR THERMO?/BIX OR DSC/BIX OR CALORIM?/
                BIX) OR ((NITRIC/BIX(W)OXIDE/BIX) OR (NO/BIX(5A)SYNTHAS?/BIX)))

L52          14 SEA FILE=WPIX ABB=ON  PLU=ON  L50 OR L51
L53          14 SEA FILE=WPIX ABB=ON  PLU=ON  L52 AND (AY<2004 OR PY<2004 OR
                PRY<2004)
L57           6 SEA FILE=WPIX ABB=ON  PLU=ON  L53 AND (?MALEAT?/BIX OR
                ?MALEIC?/BIX)
L58           0 SEA FILE=WPIX ABB=ON  PLU=ON  L53 AND ?BUTENOATE?
L59           0 SEA FILE=WPIX ABB=ON  PLU=ON  L53 AND ?BUTENOATE?/BIX
L60          14 SEA FILE=WPIX ABB=ON  PLU=ON  L53 OR (L57 OR L58 OR L59)


=> dup rem l36 l40 l60
FILE 'HCAPLUS' ENTERED AT 09:40:40 ON 24 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 09:40:40 ON 24 MAY 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 09:40:40 ON 24 MAY 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIX' ENTERED AT 09:40:40 ON 24 MAY 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L40
PROCESSING COMPLETED FOR L60
L66          20 DUP REM L36 L40 L60 (10 DUPLICATES REMOVED)
                ANSWERS '1-5' FROM FILE HCAPLUS
                ANSWERS '6-13' FROM FILE USPATFULL
                ANSWERS '14-20' FROM FILE WPIX

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 09:40:46 ON 24 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 19, 2006 (20060519/UP).
```

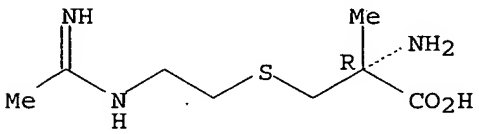
```
=> d ibib ed ab hitind hitstr
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, WPIX' - CONTINUE? (Y)/N:y


L66  ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:780659  HCAPLUS
DOCUMENT NUMBER:          141:261066
TITLE:                    S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine
                          maleate hydrochloride crystalline salt
INVENTOR(S):              Sheikh, Ahmad; Brostrom, Lyle R.; Czyzewski, Ann M.;
                          Zia, Vahid
PATENT ASSIGNEE(S):       Pharmacia Corporation, USA
SOURCE:                   PCT Int. Appl., 84 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
     WO 2004080956         A1    20040923    WO 2004-IB678          20040304 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     AU 2004220266         A1    20040923    AU 2004-220266         20040304 <--
     CA 2518745            AA    20040923    CA 2004-2518745        20040304 <--
     EP 1603872            A1    20051214    EP 2004-717188         20040304 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
     BR 2004008226         A     20060301    BR 2004-8226           20040304 <--
     US 2005038120         A1    20050217    US 2004-797462         20040310 <--
     NL 1025691            A1    20040914    NL 2004-1025691        20040311 <--
     NO 2005004645         A     20051125    NO 2005-4645           20051010 <--
PRIORITY APPLN. INFO.:                       US 2003-453496P     P  20030311 <--
                                             WO 2004-IB678       A  20040304

ED   Entered STN:  24 Sep 2004
AB   The invention relates to crystalline S-[2-[(1-iminoethyl)amino]ethyl]-
     2-methyl-L-cysteine maleate hydrochloride (I) for use in treating
     conditions characterized by an overexpression of nitric oxide from the
     inducible isoform of nitric oxide synthase.  The examples describe methods
     used to make crystalline I that may be arranged as generally orderly
     packed agglomerates, which are particularly useful in making
     pharmaceutical compns.
IC   ICM  C07C323-59
     ICS  A61K031-198; A61P029-00; C07C319-28
CC   34-2 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 63, 75
ST   iminoethylaminoethylmethylcysteine maleate hydrochloride cryst
     prepn inhibitor nitric oxide synthase; cysteine iminoethylaminoethylmethyl
     maleate hydrochloride cryst inhibitor nitric oxide synthase
```

IT **Crystallization**
Thermal analysis
X-ray diffraction
(of [[(iminoethyl)amino]ethyl]methylcysteine maleate hydrochloride **crystalline** salt)
IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of [[(iminoethyl)amino]ethyl]methylcysteine maleate hydrochloride **crystalline** salt as nitric oxide synthase inhibitor)
IT **753491-31-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of [[(iminoethyl)amino]ethyl]methylcysteine maleate hydrochloride **crystalline** salt as nitric oxide synthase inhibitor)
IT **753491-31-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of [[(iminoethyl)amino]ethyl]methylcysteine maleate hydrochloride **crystalline** salt as nitric oxide synthase inhibitor)
RN 753491-31-5 HCAPLUS
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, hydrochloride, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

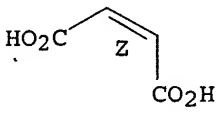
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib ed ab hitind hitstr 2-5
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, WPIX' - CONTINUE? (Y)/N:y

L66 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:780658 HCAPLUS

DOCUMENT NUMBER: 141:261065
TITLE: S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate form II **crystalline** salt
INVENTOR(S): Brostrom, Lyle R.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004080955	A1	20040923	WO 2004-IB627		20040304 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2518737	AA	20040923	CA 2004-2518737		20040304 <--
EP 1603871	A1	20051214	EP 2004-717172		20040304 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK					
BR 2004008483	A	20060404	BR 2004-8483		20040304 <--
US 2004204488	A1	20041014	US 2004-797348		20040310 <--
PRIORITY APPLN. INFO.:			US 2003-453796P	P	20030311 <--
			WO 2004-IB627	W	20040304

ED Entered STN: 24 Sep 2004

AB The invention relates to a method of preparing **crystalline** S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine (I) maleate for use in decreasing nitric oxide production in a subject. Thus, I maleate **melting** at 123 °C was obtained by **crystallization** from an acetonitrile solution Free base I was obtained by reaction of N-Boc-cysteamine (Boc = tert-butoxycarbonyl) with chloroacetone then sodium cyanide and ammonium carbonate, chromatog. separation of enantiomeric imidazolidinedione derivs., and reaction with Et acetimidate hydrochloride. **Crystalline** I maleate was **analyzed** by **X-ray** powder **diffraction** and **thermal anal.**

IC ICM C07C323-59
ICS A61K031-198; A61P029-00
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 75
ST iminoethylaminoethylmethylcysteine maleate **cryst** salt prepn property; cysteine iminoethylaminoethylmethyl maleate **cryst** salt prepn property
IT **Thermal analysis**
X-ray diffraction
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine

maleate **crystalline** salt)

IT 364068-29-1P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

IT **753480-15-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

IT 364068-31-5P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

IT 364068-30-4P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

IT 78-95-5, Chloroacetone 143-33-9, Sodium cyanide 156-57-0, 2 Aminoethanethiol hydrochloride 506-87-6, Ammonium carbonate 2208-07-3, Ethyl acetimidate hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

IT 364067-16-3P 364067-22-1P 364068-28-0P 364068-32-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

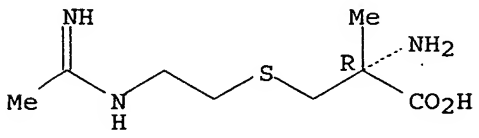
IT **753480-15-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)

RN 753480-15-8 HCAPLUS
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

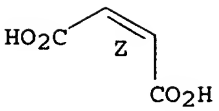
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:780657 HCAPLUS
DOCUMENT NUMBER: 141:261064
TITLE: S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate form II **crystalline** salt
INVENTOR(S): Sheikh, Ahmad; Brostrom, Lyle
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004080954	A1	20040923	WO 2004-IB697		20040304 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2517728	AA	20040923	CA 2004-2517728		20040304 <--
EP 1603869	A1	20051214	EP 2004-717175		20040304 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK					
BR 2004008177	A	20060301	BR 2004-8177		20040304 <--
US 2004209956	A1	20041021	US 2004-797500		20040310 <--
PRIORITY APPLN. INFO.:			US 2003-453782P	P	20030311 <--
			WO 2004-IB697	W	20040304

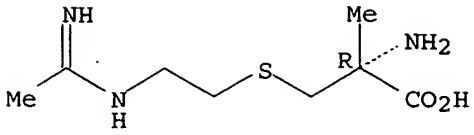
ED Entered STN: 24 Sep 2004
AB The invention relates to a method of preparing **crystalline** S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine (I) maleate for use in decreasing nitric oxide production in a subject. Thus, I maleate **melting** at 77.69 °C was obtained by **crystallization** from an acetonitrile solution Free base I was obtained by reaction of N-Boc-cysteamine (Boc = tert-butoxycarbonyl) with chloroacetone then sodium cyanide and ammonium carbonate, chromatog. separation of enantiomeric imidazolidinedione derivs., and reaction with Et acetimidate hydrochloride. **Crystalline** I maleate was **analyzed** by **X-ray** powder **diffraction** and **thermal anal.**
IC ICM C07C323-58
ICS A61K031-155; A61P029-00

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 75
ST iminoethylaminoethylmethylcysteine maleate **cryst** salt prepn property; cysteine iminoethylaminoethylmethyl maleate **cryst** salt prepn property
IT **Thermal analysis**
X-ray diffraction
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 364068-29-1P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT **753480-15-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 364068-31-5P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 364068-30-4P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 78-95-5, Chloroacetone 143-33-9, Sodium cyanide 156-57-0, 2 Aminoethanethiol hydrochloride 506-87-6, Ammonium carbonate 2208-07-3, Ethyl acetimidate hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT 364067-16-3P 364067-22-1P 364068-28-0P 364068-32-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
IT **753480-15-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate **crystalline** salt)
RN 753480-15-8 HCAPLUS
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

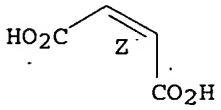
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2001:730698 HCAPLUS
DOCUMENT NUMBER: 135:289056
TITLE: Preparation of amidino compounds useful as nitric oxide synthase inhibitors
INVENTOR(S): Webber, Ronald Keith; Awasthi, Alok K.; Bergmanis, Arija A.; Durley, Richard C.; Ganser, Scott S.; Hagen, Timothy J.; Hallinan, Ann E.; Hansen, Donald W.; Hickory, Brian S.; Moormann, Alan E.; Pitzele, Barnett S.; Promo, Michelle A.; Schartman, Richard R.; Snyder, Jeffrey S.; Trivedi, Mahima; Tsymbalov, Sofya
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072703	A1	20011004	WO 2001-US9433	20010323 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402436	AA	20011004	CA 2001-2402436	20010323 <--
US 2002019563	A1	20020214	US 2001-816577	20010323 <--
US 6403830	B2	20020611		
US 2002111493	A1	20020815	US 2001-816575	20010323 <--

US 6586474	B2	20030701			
EP 1265860	A1	20021218	EP 2001-922636		20010323 <--
EP 1265860	B1	20050518			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001009386	A	20030415	BR 2001-9386		20010323 <--
ZA 2002006459	A	20030813	ZA 2002-6459		20010323 <--
JP 2003528853	T2	20030930	JP 2001-570616		20010323 <--
NZ 520812	A	20040430	NZ 2001-520812		20010323 <--
AT 295832	E	20050615	AT 2001-922636		20010323 <--
ES 2240445	T3	20051016	ES 2001-1922636		20010323 <--
PT 1265860	T	20051031	PT 2001-922636		20010323 <--
ZA 2002006455	A	20030813	ZA 2002-6455		20020813 <--
US 2003199701	A1	20031023	US 2002-321969		20021217 <--
US 2004186178	A1	20040923	US 2004-815375		20040401 <--
US 6914158	B2	20050705			
US 2005165106	A1	20050728	US 2005-32650		20050110 <--
PRIORITY APPLN. INFO.:			US 2000-191923P	P	20000324 <--
			US 2001-816575	A3	20010323 <--
			WO 2001-US9433	W	20010323 <--
			US 2002-321969	B3	20021217 <--
			US 2004-815375	A1	20040401

OTHER SOURCE(S): MARPAT 135:289056
ED Entered STN: 07 Oct 2001
AB The invention relates to S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine (1) or its pharmaceutically acceptable salts for use as nitric oxide synthase (NOS) inhibitors. Thus, 1.2HCl was prepared by a multistep procedure involving S-alkylation of (2R)-2-methyl-L-cysteine hydrochloride with Boc-NHCH2CH2Br (Boc = tert-butoxycarbonyl), deprotection, condensation with Et acetimidate hydrochloride, and acidolysis with 1 N HCl. (2R)-2-methyl-L-cysteine hydrochloride was obtained from (R)-cysteine Me ester hydrochloride. Inhibitory assays for compound 1.2HCl showed hiNOS, hecNOS, hncNOS, and human cartilage IC50 values 3.1, 77, 15 μM, and 0.7 μM, resp.
IC ICM C07C323-58
ICS A61K031-155; A61P029-00
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
IT 5962-42-5DP, calcium and lithium complexes 7439-93-2DP, Lithium, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine complexes, preparation 7440-66-6DP, Zinc, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine complexes, preparation 7440-70-2DP, Calcium, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine complexes, preparation 364067-17-4P 364067-18-5P 364067-19-6P 364067-20-9P 364067-21-0P 364067-22-1DP, IPR (amberlite)-69 salt 364067-22-1DP, calcium and zinc complexes 364067-22-1P 364067-23-2P 364067-24-3P 364067-25-4P 364067-26-5P 364067-27-6P 364067-28-7P 364067-30-1P 364067-31-2P 364067-32-3P 364067-33-4P 364067-38-9P 364067-39-0P 364067-40-3P 364067-41-4P 364067-42-5P 364067-43-6P 364067-44-7P 364067-45-8P 364067-46-9P 364067-47-0P 364067-48-1P 364067-49-2P 364067-50-5P 364067-51-6P 364067-52-7P 364067-53-8P 364067-54-9P 364067-55-0P 364067-56-1P 364067-57-2P 364067-58-3P 364067-59-4P 364067-60-7P 364067-61-8P 364067-62-9P 364067-64-1P 364067-65-2P 364067-66-3P 364067-67-4P 364067-68-5P 364067-69-6P 364067-70-9P 364067-71-0P 364067-72-1P 364067-73-2P 364067-74-3P 364067-75-4P 364067-76-5P 364067-77-6P 364067-78-7P 364067-79-8P **364067-80-1P** 364067-81-2P 364067-82-3P 364067-83-4P 364067-84-5P 364067-85-6P 364067-86-7P 364067-87-8P 364067-88-9P 364067-89-0P 364067-90-3P 364067-91-4P 364067-92-5P 364067-93-6P 364067-94-7P 364067-95-8P 364067-96-9P 364067-97-0P 364067-98-1P

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364081-92-5P 364081-93-6P 364081-94-7P 364081-95-8P 364081-96-9P
364081-97-0P 364081-98-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)

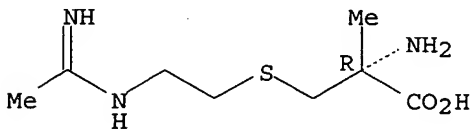
IT **364067-80-1P 364068-09-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)

RN 364067-80-1 HCAPLUS
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

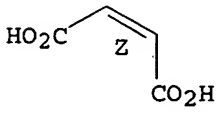
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

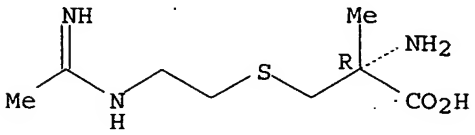


RN 364068-09-7 HCAPLUS
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

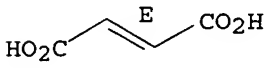
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2001:730697 HCAPLUS
DOCUMENT NUMBER: 135:273215
TITLE: Preparation of amidino compounds useful as nitric oxide synthase inhibitors
INVENTOR(S): Webber, Ronald Keith; Awasthi, Alok K.; Bergmanis, Arija A.; Durley, Richard C.; Fok, Kam F.; Ganser, Scott S.; Hagen, Timothy J.; Hallinan, Ann E.; Hansen, Donald W.; Hickory, Brian S.; Manning, Pamela T.; Mao, Michael; Moormann, Alan E.; Pitzele, Barnett S.; Promo, Michelle A.; Schartman, Richard R.; Scholten, Jeffrey A.; Snyder, Jeffrey S.; Toth, Mihaly V.; Trivedi, Mahima; Tsymbalov, Sofya; Tjoeng, Foe Siong
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072702	A2	20011004	WO 2001-US9431	20010323 <--
WO 2001072702	A3	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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US 6586474	B2	20030701		
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US 6914158	B2	20050705		
US 2005165106	A1	20050728	US 2005-32650	20050110 <--

PRIORITY APPLN. INFO.:	US 2000-191923P	P	20000324 <--
	US 2001-816575	A3	20010323 <--
	WO 2001-US9431	W	20010323 <--
	US 2002-321969	B3	20021217 <--
	US 2004-815375	A1	20040401

OTHER SOURCE(S): MARPAT 135:273215

ED Entered STN: 07 Oct 2001

AB Amidino compds. R11N:CR13NR12CR9R10CR1R7-X-CR5R6CR2(NR3R4)COR8 [X = S, SO, SO2; R1, R5, R6, R7 = H, halo, alkyl (alkyl and other groups may be substituted), alkenyl, alkynyl, alkoxyalkyl; R2 = alkyl, alkenyl, alkynyl, alkoxyalkyl, alkylthioalkyl; R3 = H, OH, CHO, alkanoyl, CO2H, C(O)SH or alkyl esters; R8 = OH, alkoxy, an amino or alkylamino group or R3 and R8 may form a ring; R4 = H, CO2H, carbalkoxy; R9, R10 = H, alkyl, alkenyl, alkynyl, alkoxyalkyl; R11, R12 = H, OH, CO2H, C(O)SH or esters or R11 and R12 may form a ring; R13 = alkyl (with provisos)] or their salts were prepared as nitric oxide synthase (NOS) inhibitors. Thus, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine dihydrochloride (1) was prepared by a multistep procedure involving S-alkylation of (2R)-2-methyl-L-cysteine hydrochloride with Boc-NHCH2CH2Br (Boc = tert-butoxycarbonyl), deprotection, condensation with Et acetimidate hydrochloride, and acidolysis with 1 N HCl. (2R)-2-methyl-L-cysteine hydrochloride was obtained from (R)-cysteine Me ester hydrochloride. Inhibitory assays for compound 1 showed hiNOS, hecNOS, hncNOS, and human cartilage IC50 values 3.1, 77, 15 μM, and 0.7 μM, resp.

IC ICM C07C323-58
ICS C07C317-48; C07D271-06; C07D233-76; C07C323-59; A61K031-155; A61P029-00

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT 5962-42-5DP, calcium and lithium complexes 7439-93-2DP, Lithium, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine complexes, preparation 7440-66-6DP, Zinc, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine complexes, preparation 7440-70-2DP, Calcium, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine complexes, preparation 364067-17-4P 364067-18-5P 364067-19-6P 364067-20-9P 364067-21-0P 364067-22-1DP, IPR (amberlite)-69 salt 364067-22-1DP, calcium and zinc complexes 364067-22-1P 364067-23-2P 364067-24-3P

364067-25-4P 364067-26-5P 364067-27-6P 364067-28-7P 364067-30-1P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)

IT **364067-80-1P 364068-09-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)

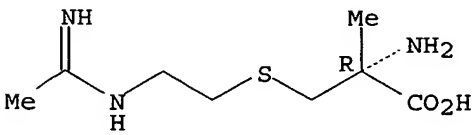
RN 364067-80-1 HCAPLUS

CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

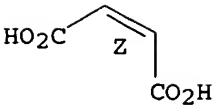
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

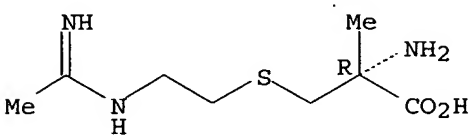


RN 364068-09-7 HCAPLUS
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

Absolute stereochemistry.



CM 2

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CMF C4 H4 O4

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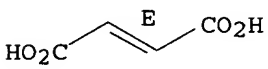

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L66 ANSWER 6 OF 20 USPATFULL on STN DUPLICATE 4
ACCESSION NUMBER: 2004:240363 USPATFULL
TITLE: Amidino compounds useful as nitric oxide synthase inhibitors
INVENTOR(S): Webber, Ronald Keith, St. Charles, MO, UNITED STATES
Durley, Richard C., Chesterfield, MO, UNITED STATES
Awasthi, Alok K., Skokie, IL, UNITED STATES
Bergmanis, Arija A., Des Plaines, IL, UNITED STATES
Fok, Kam F., St. Louis, MO, UNITED STATES
Ganser, Scott S., Chicago, IL, UNITED STATES
Hagen, Timothy J., Gurne, IL, UNITED STATES
Hallinan, E. Ann, Evanston, IL, UNITED STATES
Hansen, Donald W., JR., Skokie, IL, UNITED STATES
Hickory, Brian S., Wildwood, MO, UNITED STATES
Manning, Pamela T., Labadie, MO, UNITED STATES
Mao, Michael, Chesterfield, MO, UNITED STATES

Moormann, Alan E., Weldon Springs, MO, UNITED STATES
Pitzele, Barnett S., Skokie, IL, UNITED STATES
Promo, Michelle A., Chesterfield, MO, UNITED STATES
Schartman, Richard R., Evanston, IL, UNITED STATES
Scholten, Jeffrey A., Chesterfield, MO, UNITED STATES
Snyder, Jeffrey S., Manchester, MO, UNITED STATES
Toth, Mihaly V., St. Louis, MO, UNITED STATES
Trivedi, Mahima, Glenview, IL, UNITED STATES
Tsymabalov, Sofya, Skokie, IL, UNITED STATES
Tjoeng, Foe Siong, Ballwin, MO, UNITED STATES
PATENT ASSIGNEE(S): Pharmacia Corporation, St. Louis, MO (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004186178	A1	20040923
	US 6914158	B2	20050705
APPLICATION INFO.:	US 2004-815375	A1	20040401 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2002-321969, filed on 17 Dec 2002, ABANDONED Division of Ser. No. US 2001-816575, filed on 23 Mar 2001, GRANTED, Pat. No. US 6586474

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-191923P	20000324 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pfizer Corporate Patent Department, P. O. Box 1027, Chesterfield, MO, 63006
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 3249
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

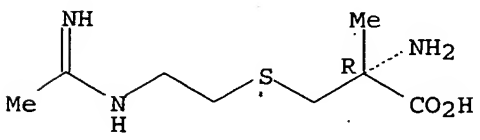
AB The present invention relates to amidino compounds and salts and prodrugs thereof. In another embodiment the present invention also provides a use of the present compounds in therapy, particular as nitric oxide synthase inhibitors. In a further embodiment, the present invention provides methods of making the amidino compounds.

IT **364067-80-1P 364068-09-7P**
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)
RN 364067-80-1 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

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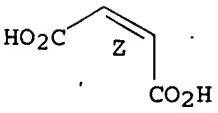
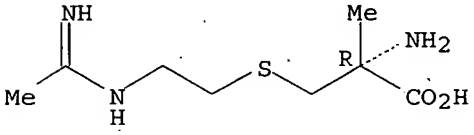


RN 364068-09-7 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

Absolute stereochemistry.



CM 2

CRN 110-17-8
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CDES 2:E

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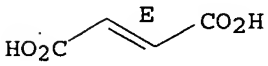


L66 ANSWER 7 OF 20 USPATFULL on STN DUPLICATE 5
ACCESSION NUMBER: 2002:206792 USPATFULL
TITLE: Amidino compounds useful as nitric oxide synthase inhibitors
INVENTOR(S): Webber, Ronald Keith, St. Charles, MO, UNITED STATES
Awasthi, Alok K., Skokie, IL, UNITED STATES
Bergmanis, Arija A., Des Plaines, IL, UNITED STATES
Durley, Richard C., Chesterfield, MO, UNITED STATES
Fok, Kam F., St. Louis, MO, UNITED STATES
Ganser, Scott S., Chicago, IL, UNITED STATES
Hagen, Timothy J., Gurne, IL, UNITED STATES
Hallinan, E. Ann, Evanston, IL, UNITED STATES
Hansen, Donald W., JR., Skokie, IL, UNITED STATES
Hickory, Brian S., Wildwood, MO, UNITED STATES
Manning, Pamela T., Labadie, MO, UNITED STATES
Mao, Michael, Chesterfield, MO, UNITED STATES

Moormann, Alan E., Weldon Springs, MO, UNITED STATES
Pitzele, Barnett S., Skokie, IL, UNITED STATES
Promo, Michelle A., Chesterfield, MO, UNITED STATES
Schartman, Richard R., Evanston, IL, UNITED STATES
Scholten, Jeffrey A., Chesterfield, MO, UNITED STATES
Snyder, Jeffrey S., Manchester, MO, UNITED STATES
Toth, Mihaly V., St. Louis, MO, UNITED STATES
Trivedi, Mahima, Glenview, IL, UNITED STATES
Tsymbalov, Sofya, Skokie, IL, UNITED STATES
Tjoeng, Foe Siong, Ballwin, MO, UNITED STATES

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2002111493	A1	20020815		<--
	US 6586474	B2	20030701		
APPLICATION INFO.:	US 2001-816575	A1	20010323	(9)	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-191923P	20000324	(60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pharmicia Corporation, Corporate Patent Department, P.O. Box 5110, Chicago, IL, 60680-9889
NUMBER OF CLAIMS: 221
EXEMPLARY CLAIM: 1
LINE COUNT: 4032
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

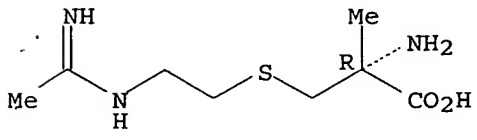
AB The present invention relates to amidino compounds and salts and prodrugs thereof. In another embodiment the present invention also provides a use of the present compounds in therapy, particular as nitric oxide synthase inhibitors. In a further embodiment, the present invention provides methods of making the amidino compounds.

IT **364067-80-1P 364068-09-7P**
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)
RN 364067-80-1 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

Absolute stereochemistry.



CM 2

CRN 110-16-7
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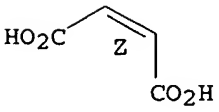
CDES 2:Z

Double bond geometry as shown.

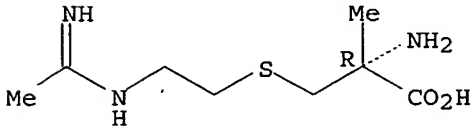


RN 364068-09-7 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

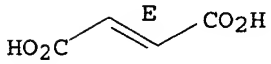
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L66 ANSWER 8 OF 20 USPATFULL on STN DUPLICATE 6
ACCESSION NUMBER: 2002:32739 USPATFULL
TITLE: Amidino compound and salts thereof useful as nitric oxide synthase inhibitors
INVENTOR(S): Webber, Ronald Keith, St. Charles, MO, UNITED STATES
Durley, Richard C., Chesterfield, MO, UNITED STATES
Awasthi, Alok K., Skokie, IL, UNITED STATES
Bergmanis, Arija A., Des Plaines, IL, UNITED STATES
Ganser, Scott S., Chicago, IL, UNITED STATES
Hagen, Timothy J., Gurne, IL, UNITED STATES
Hallinan, E. Ann, Evanston, IL, UNITED STATES
Hansen, Donald W., JR., Skokie, IL, UNITED STATES
Hickory, Brian S., Wildwood, MO, UNITED STATES
Moormann, Alan E., Weldon Springs, MO, UNITED STATES
Pitzele, Barnett S., Skokie, IL, UNITED STATES
Promo, Michelle A., Chesterfield, MO, UNITED STATES
Schartman, Richard R., Evanston, IL, UNITED STATES
Snyder, Jeffrey S., Manchester, MO, UNITED STATES
Trivedi, Mahima, Glenview, IL, UNITED STATES
Tsymbalov, Sofya, Skokie, IL, UNITED STATES

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2002019563	A1	20020214		<--
	US 6403830	B2	20020611		
APPLICATION INFO.:	US 2001-816577	A1	20010323	(9)	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-191923P	20000324 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pharmacia Corporation, Corporate Patent Department, P.O. Box 5110, Chicago, IL, 60680-9889
NUMBER OF CLAIMS: 39
EXEMPLARY CLAIM: 1
LINE COUNT: 3313
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine, or a pharmaceutically acceptable salt thereof.

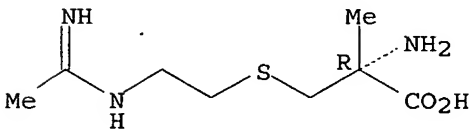
IT **364067-80-1P 364068-09-7P**
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)

RN 364067-80-1 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

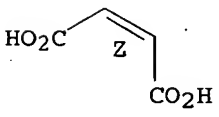
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.

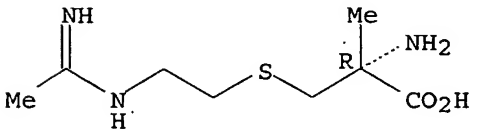


RN 364068-09-7 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

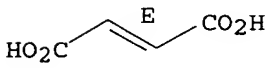
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L66 ANSWER 9 OF 20 USPATFULL on STN

ACCESSION NUMBER:	2005:190190 USPATFULL
TITLE:	Amidino compounds useful as nitric oxide synthase inhibitors
INVENTOR(S):	Webber, Ronald Keith, St. Charles, MO, UNITED STATES Durley, Richard C., Chesterfield, MO, UNITED STATES Awasthi, Alok K., Skokie, IL, UNITED STATES Bergmanis, Arijia A., Des Plaines, IL, UNITED STATES Fok, Kam F., St. Louis, MO, UNITED STATES Ganser, Scott S., Chicago, IL, UNITED STATES Hagen, Timothy J., Gurne, IL, UNITED STATES Hallinan, E. Ann, Evanston, IL, UNITED STATES Hansen, Donald W. JR., Skokie, MO, UNITED STATES Hickory, Brian S., Wildwood, MO, UNITED STATES Manning, Pamela T., Labadie, MO, UNITED STATES Mao, Michael, Chesterfield, MO, UNITED STATES Moormann, Alan E., Weldon Springs, MO, UNITED STATES Pitzele, Barnett S., Skokie, IL, UNITED STATES Promo, Michelle A., Chesterfield, MO, UNITED STATES Schartman, Richard R., Evanston, IL, UNITED STATES Scholten, Jeffrey A., Chesterfield, MO, UNITED STATES Snyder, Jeffrey S., Manchester, MO, UNITED STATES Toth, Mihaly V., St. Louis, MO, UNITED STATES Trivedi, Mahima, Glenview, IL, UNITED STATES Tsymbalov, Sofya, Skokie, IL, UNITED STATES Tjoeng, Foe Siong, Ballwin, MO, UNITED STATES
PATENT ASSIGNEE(S):	Pharmacia Corporation, St. Louis, MO, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005165106	A1	20050728	
APPLICATION INFO.:	US 2005-32650	A1	20050110	(11)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2004-815375, filed on 1 Apr 2004, PENDING Division of Ser. No. US 2002-321969, filed on 17 Dec 2002, ABANDONED Division of Ser. No. US 2001-816575, filed on 23 Mar 2001, GRANTED, Pat. No. US 6586474

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-191923P	20000324 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pfizer Corporate Patent Department, P.O. Box 1027, Chesterfield, MO, 63006, US
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 3260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to amidino compounds and salts and prodrugs thereof. In another embodiment the present invention also provides a use of the present compounds in therapy, particular as nitric oxide synthase inhibitors. In a further embodiment, the present invention provides methods of making the amidino compounds.

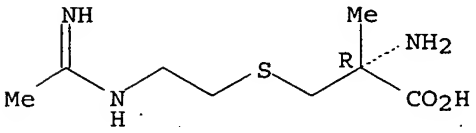
IT **364067-80-1P 364068-09-7P**
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)

RN 364067-80-1 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

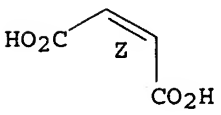
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.

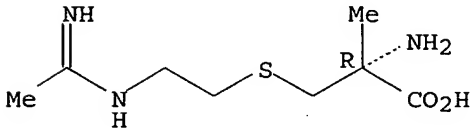


RN 364068-09-7 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

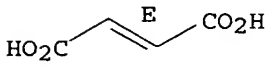
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L66 ANSWER 10 OF 20 USPATFULL on STN

ACCESSION NUMBER:	2005:44387 USPATFULL
TITLE:	S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride crystalline salt
INVENTOR(S):	Brostrom, Lyle, Lincolnshire, IL, UNITED STATES Czyzewski, Ann, Grayslake, IL, UNITED STATES Zia, Vahid, San Francisco, CA, UNITED STATES Sheikh, Ahmad, Dearfield, IL, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005038120	A1	20050217	
APPLICATION INFO.:	US 2004-797462	A1	20040310	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-453496P	20030311 (60)	<--

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Pharmacia Corporation, Corporate Patent Department, P.O. Box 1027, Chesterfield, MO, 63006
NUMBER OF CLAIMS:	15
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	11 Drawing Page(s)
LINE COUNT:	2872

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel mixed salt of S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine is disclosed. The novel mixed salt, S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride, may be produced to form crystals that may be arranged as generally orderly packed agglomerates, which are particularly useful in making

pharmaceutical compositions. Such pharmaceutical compositions are also described, as well as methods to make crystalline S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride, and methods of treating conditions characterized by an overexpression on nitric oxide from the inducible isoform of nitric oxide synthase using the S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate hydrochloride.

IT **753491-31-5P**
(preparation of [[(iminoethyl)amino]ethyl]methylcysteine maleate hydrochloride crystalline salt as nitric oxide synthase inhibitor)

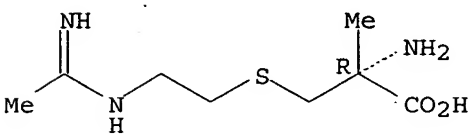
RN 753491-31-5 USPATFULL

CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, hydrochloride, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

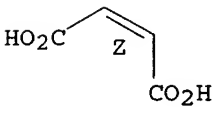
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



L66 ANSWER 11 OF 20 USPATFULL on STN

ACCESSION NUMBER:	2004:268413 USPATFULL
TITLE:	S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate form II crystalline salt
INVENTOR(S):	Brostrom, Lyle, Lincolnshire, IL, UNITED STATES Sheikh, Ahmad, Dearfield, IL, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004209956	A1	20041021	
APPLICATION INFO.:	US 2004-797500	A1	20040310	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-453782P	20030311 (60)	<--

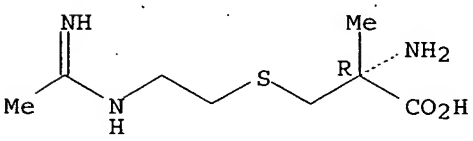
DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pharmacia Corporation, Corporate Patent Department, P.O. Box 1027, Chesterfield, MO, 63006
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 1727
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Form II crystalline maleate salt of S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine is disclosed. The Form II crystalline salt is a channel hydrate, with a melting point of about 77.69° C.
IT **753480-15-8P**
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate crystalline salt)
RN 753480-15-8 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

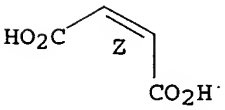
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



L66 ANSWER 12 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2004:261986 USPATFULL
TITLE: S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine maleate crystalline salt
INVENTOR(S): Brostrom, Lyle, Lincolnshire, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004204488	A1	20041014
APPLICATION INFO.:	US 2004-797348	A1	20040310 (10)

NUMBER DATE

PRIORITY INFORMATION: US 2003-453796P 20030311 (60) <--
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pharmacia Corporation, Corporate Patent Department, P.O. Box 1027, Chesterfield, MO, 63006
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 1506
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A crystalline maleate salt of S-[2-[(1-Iminoethyl)amino]ethyl]-2-methyl-L-cysteine is disclosed. The crystalline salt has absorption of less than one percent water by weight at 90% R.H. at 25° C., a melting point of 123° C., and aqueous solubility in excess of 230 mg ml.sup.-1.

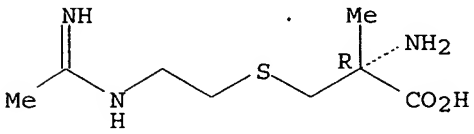
IT **753480-15-8P**
(preparation and properties of [[(iminoethyl)amino]ethyl]methylcysteine maleate crystalline salt)

RN 753480-15-8 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

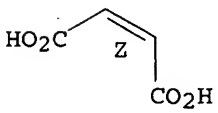
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



L66 ANSWER 13 OF 20 USPATFULL on STN
ACCESSION NUMBER: 2003:283357 USPATFULL
TITLE: Methods of making amidino compounds useful as nitric oxide synthase inhibitors
INVENTOR(S): Webber, Ronald Keith, St. Charles, MO, UNITED STATES
Durley, Richard C., Chesterfield, MO, UNITED STATES
Awasthi, Alok K., Skokie, IL, UNITED STATES

Bergmanis, Arija A., Des Plaines, IL, UNITED STATES
Fok, Kam F., St. Louis, MO, UNITED STATES
Ganser, Scott S., Chicago, IL, UNITED STATES
Hagen, Timothy J., Gurne, IL, UNITED STATES
Hallinan, E. Ann, Evanston, IL, UNITED STATES
Hansen, Donald W., JR., Skokie, IL, UNITED STATES
Hickory, Brian S., Wildwood, MO, UNITED STATES
Manning, Pamela T., Labadie, MO, UNITED STATES
Mao, Michael, Chesterfield, MO, UNITED STATES
Moormann, Alan E., Weldon Springs, MO, UNITED STATES
Pitzele, Barnett S., Skokie, IL, UNITED STATES
Promo, Michelle A., Chesterfield, MO, UNITED STATES
Schartman, Richard R., Evanston, IL, UNITED STATES
Scholten, Jeffrey A., Chesterfield, MO, UNITED STATES
Snyder, Jeffrey S., Manchester, MO, UNITED STATES
Toth, Mihaly V., St. Louis, MO, UNITED STATES
Trivedi, Mahima, Glenview, IL, UNITED STATES
Tsymbalov, Sofya, Skokie, IL, UNITED STATES
Tjoeng, Foe Siong, Ballwin, MO, UNITED STATES
PATENT ASSIGNEE(S): Pharmacia Corporate, Chicago, IL (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003199701	A1	20031023	<--
APPLICATION INFO.:	US 2002-321969	A1	20021217 (10)	<--

RELATED APPLN. INFO.: Division of Ser. No. US 2001-816575, filed on 23 Mar 2001, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-191923P	20000324 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pharmacia Corporation, Corporate Patent Department, 800 North Lindbergh Blvd., Mail Zone O4E, St. Louis, MO, 63167
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 3259
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of making an alpha-amino acid compound having the structure of Formula 32: ##STR1##

comprising treating under hydrolyzing conditions a hydantoin compound having the structure of Formula 33: ##STR2##

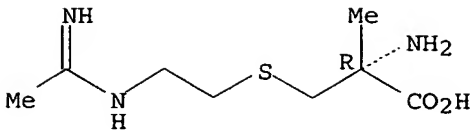
where the substituents are described herein.

IT **364067-80-1P 364068-09-7P**
(preparation of amidino compds. useful as nitric oxide synthase inhibitors)
RN 364067-80-1 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2Z)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

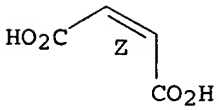
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.

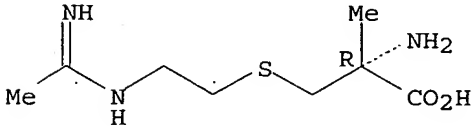


RN 364068-09-7 USPATFULL
CN L-Cysteine, S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 364067-22-1
CMF C8 H17 N3 O2 S

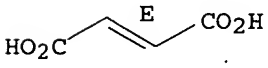
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



=> d iall abeq tech abex hitstr 14
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, WPIX' - CONTINUE? (Y)/N:y

L66 ANSWER 14 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-253851 [26] WPIX
DOC. NO. CPI: C2005-080379
TITLE: Composition, useful for the treatment of cancer e.g. adrenocortical carcinoma, head and neck cancer, comprises administering carbamoylating chemotherapeutic agent in combination with selective inducible **nitric oxide** synthase inhibitor.
DERWENT CLASS: B05
INVENTOR(S): HSU, C Y; MANNING, P T; MISKO, T P
PATENT ASSIGNEE(S): (HSUC-I) HSU C Y; (MANN-I) MANNING P T; (MISK-I) MISKO T P; (PHAA) PHARMACIA CORP
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005025620	A2	20050324	(200526)*	EN	200	A61K045-06
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 2005203082	A1	20050915	(200561)			A61K031-55

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
WO 2005025620	A2	WO 2004-US26394	20040813	
US 2005203082	A1 Provisional	US 2003-494917P	20030813	<--
		US 2004-918535	20040813	

PRIORITY APPLN. INFO: **US 2003-494917P 20030813**; US 2004-918535 20040813
INT. PATENT CLASSIF.:
MAIN: A61K031-55; A61K045-06
SECONDARY: A61K031-53; A61P035-00
BASIC ABSTRACT:
WO2005025620 A UPAB: 20050422
NOVELTY - Treatment of cancer comprises administration of carbamoylating chemotherapeutic agent (I) in combination with a selective inducible **nitric oxide** synthase (iNOS) inhibitor (II).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit comprising (I) and (II) or its salts.
ACTIVITY - Cytostatic.
MECHANISM OF ACTION - Inducible **nitric oxide** synthase inhibitor (iNOS).
In a citrulline assay for human inducible NOS (hiNOS), results showed that (2S,5E)-2-amino-6-fluoro-7-((1-iminoethyl)amino)-5-heptenoic acid, dihydrochloride, monohydrate (IIa) exhibited an IC50 value of 0.36 mu M.
USE - Compound (I), in combination with (II), is useful for the treatment of cancers (adrenocortical carcinoma, cerebellar astrocytoma, brain stem glioma, ependymoma, medulloblastoma, supratentorial primitive neuroectodermal and pineal tumors, visual pathway and hypothalamic gliomas, astrocytomas including glioblastoma multiforme, primary central

nervous system lymphoma, eye cancers including intraocular melanoma and retinoblastoma, head and neck cancer, neuroblastoma, pituitary tumor, meningioma, primitive neuroectodermal tumor and secondary brain tumor) and in the treatment of neoplasias resistant to (I) (all claimed).

ADVANTAGE - The treatment using (I) in combination with (II) is robust and relatively safe, as well as effective for protracted periods of time.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B05-A03B; B05-B01E; B06-H; B07-H; B10-A09B; B10-A12B; B10-A13D; B10-A17; B10-B02H; B14-D10; B14-H01; B14-S09

TECH UPTX: 20050422

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The use of 12 generic compounds (II) are claimed in the specification e.g.
Me-C(=NR7)-NH-CH2-C(R1)=C(R2)-CH2CH2-CH(NH2)-CO-J (IIA).
R1, R2 = H, halo or alkyl (optionally substituted by halo);
R7 = H or OH;
J = OH, alkoxy or NR3R4;
R3 = H, lower alkyl, lower alkylenyl or lower alkynyl, and
R4 = H, heterocyclyl containing 1-4 O, N or S heteroatoms (optionally substituted by heteroarylamino, N-aryl-N-alkylamino, N-heteroarylamino-N-alkylamino, haloalkylthio, alkanoyloxy, alkoxy, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, cyanoalkyl, dicyanoalkyl, carboxamidoalkyl, dicarboxamidoalkyl, cyanocarboalkoxyalkyl, carboalkoxyalkyl, dicarboalkoxyalkyl, cyanocycloalkyl, dicyanocycloalkyl, carboxamidocycloalkyl, dicarboxamidocycloalkyl, carboalkoxycyanocycloalkyl, carboalkoxycycloalkyl, dicarboalkoxycycloalkyl, formylalkyl, acylalkyl, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, phosphonoalkyl, dialkoxyphosphonoalkoxy, diaralkoxyphosphonoalkoxy, phosphonoalkoxy, dialkoxyphosphonoalkylamino,diaralkoxyphosphonoalkylamino, phosphonoalkylamino, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, guanidino, amidino or acylamino).
Compound (I) is an alkylating agent. (I) comprises carmustine, lomustine, methyl lomustine, cyclodisone, clomesone, L-cysteine analog of formula (IA), 2,4-diamino-6,6-dimethyl-1-(3-dimethylaminocarbonylbenzyloxy)-1,3,5-triazine, triazinate, mitozolomide, carboplatin or chlorozotocin.

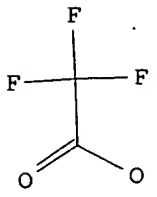
ABEX UPTX: 20050422

SPECIFIC COMPOUNDS - The use of 40 compounds (II) is specifically claimed e.g. (2S,5E)-2-amino-6-fluoro-7-((1-iminoethyl)amino)-5-heptenoic acid, dihydrochloride, monohydrate (IIa).

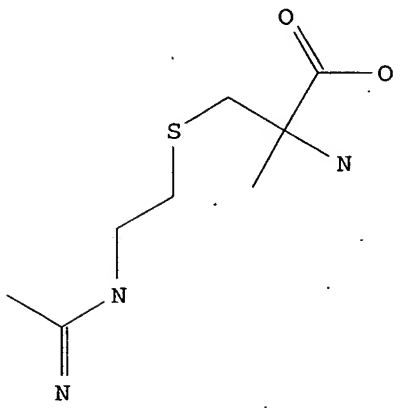
ADMINISTRATION - The dosage of (II) is 0.001-2500 mg/kg/day intranasally, mucosally, orally, intravenously, subcutaneously, rectally, topically, buccally, sublingually, intramuscularly, intradermally or via inhalation.

DCSE 831193-0-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with trifluoro-acetic acid
SDCN RACSJU

CM 1



CM 2

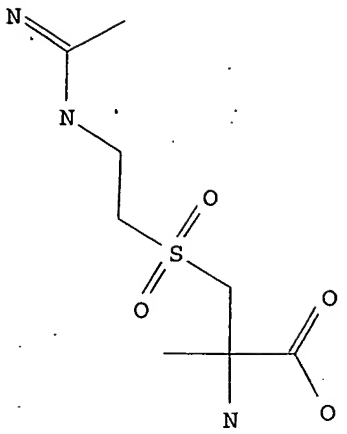


DCSE 478306-0-1-0
CN.S 3-(2-Acetimidoylamino-ethanesulfonyl)-2-amino-2-methyl-propionic acid; hydrochloride
SDCN RACSJY

CM 1

Cl

CM 2

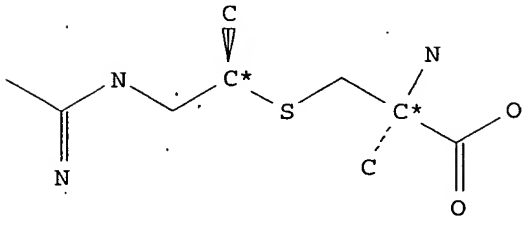


DCSE 478285-1-3-0
CN.S 3-(2-Acetimidoylamino-1-methyl-ethylsulfanyl)-2-amino-2-methyl-propionic acid dihydrochloride
SDCN RAHF7P

CM 1

Cl

CM 2

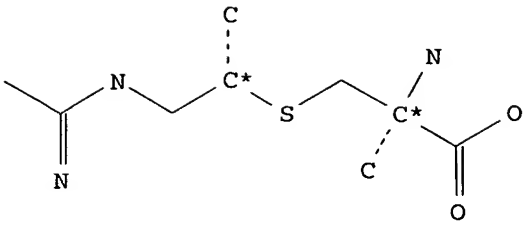


DCSE 478285-5-4-0
CN.S 3-(2-Acetimidoylamino-1-methyl-ethylsulfanyl)-2-amino-2-methyl-propionic acid dihydrochloride
SDCN RAHF7Q

CM 1

Cl

CM 2

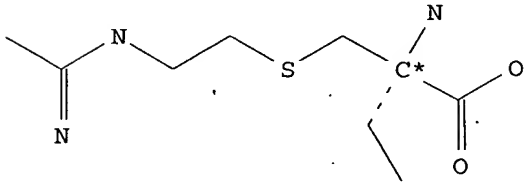


DCSE 478290-3-2-0
CN.S 2-(2-Acetimidoylamino-ethylsulfanylmethyl)-2-amino-butyric acid dihydrochloride
SDCN RAHF7S

CM 1

Cl

CM 2

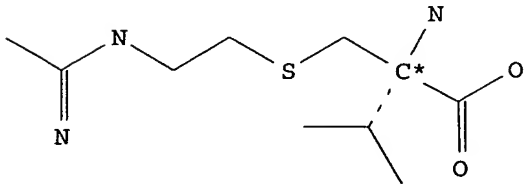


DCSE 478296-1-2-0
CN.S 2-(2-Acetimidoylamino-ethylsulfanylmethyl)-2-amino-3-methyl-butyric acid dihydrochloride
SDCN RAHF7T

CM 1

Cl

CM 2



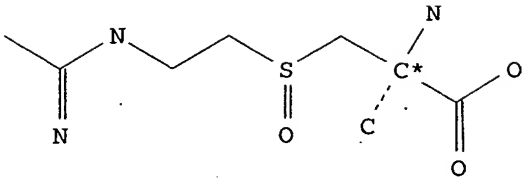
DCSE 478305-2-1-0
CN.S 3-(2-Acetimidoylamino-ethanesulfinyl)-2-amino-2-methyl-propionic acid dihydrochloride

SDCN RAHF7V

CM 1

Cl

CM 2

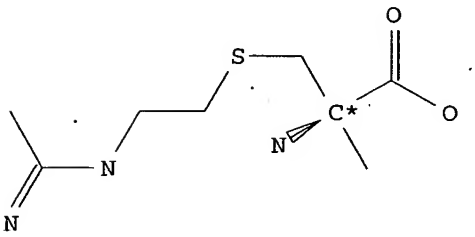


DCSE 962301-1-3-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with GENERIC INORGANIC NEUTRAL COMPONENT
SDCN RAFIL7

CM 1

Cl

CM 2



=> d iall abeq tech abex hitstr 15-20
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, USPATFULL, WPIX' - CONTINUE? (Y)/N:y

L66 ANSWER 15 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-690590 [67] WPIX
DOC. NO. CPI: C2004-244756
TITLE: Removing counterions from salt compound useful for preparing ionic salts, which are useful for treating e.g. arthritis involves contacting the compound in solution with ion exchange medium and separating the solution containing the compound.

DERWENT CLASS: A96 B03 B05
INVENTOR(S): MOORE, C; MOORE, C J
PATENT ASSIGNEE(S): (PHAA) PHARMACIA CORP; (MOOR-I) MOORE C; (PFIZ) PFIZER INC
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004081073	A2	20040923	(200467)*	EN	28	C08G000-00
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 2004225150	A1	20041111	(200475)			C07C323-25
EP 1603671	A2	20051214	(200582)	EN		B01J039-04
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
US 6995281	B2	20060207	(200611)			C07C323-00
BR 2004008275	A	20060307	(200619)			B01J039-04
MX 2005009244	A1	20051101	(200625)			B01D061-38

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
WO 2004081073	A2	WO 2004-IB529	20040223	
US 2004225150	A1 Provisional	US 2003-453798P	20030311	<--
		US 2004-797350	20040310	
EP 1603671	A2	EP 2004-713607	20040223	
		WO 2004-IB529	20040223	
US 6995281	B2 Provisional	US 2003-453798P	20030311	<--
		US 2004-797350	20040310	
BR 2004008275	A	BR 2004-8275	20040223	
		WO 2004-IB529	20040223	
MX 2005009244	A1	WO 2004-IB529	20040223	
		MX 2005-9244	20050830	

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1603671	A2 Based on	WO 2004081073
BR 2004008275	A Based on	WO 2004081073
MX 2005009244	A1 Based on	WO 2004081073

PRIORITY APPLN. INFO: **US 2003-453798P 20030311**; US 2004-797350 20040310
INT. PATENT CLASSIF.:
MAIN: B01D061-38; B01J039-04; C07C323-00; C07C323-25; C08G000-00
SECONDARY: B01J041-04; C07B063-00; C07C257-14; C07C319-20; C07C323-59
BASIC ABSTRACT:
WO2004081073 A UPAB: 20041019
NOVELTY - Removing counterions from a salt compound involves contacting

the compound in solution with ion exchange medium and separating the solution containing the compound from the ion medium.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) preparation of S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine zwitterion having 0 - 2 (preferably less than 0.5) equivalents of hydrochloride ion involving obtaining a source of S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine dihydrochloride and removing hydrochloride acid preferably using resin in a column; and

(2) new intermediate, S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine.

ACTIVITY - Antiinflammatory; Cardiant; Cardiovascular-Gen.; Antidiabetic; Antiarteriosclerotic; Ophthalmological; Antiasthmatic; Antimigraine; Antidiarrheic; Gastrointestinal-Gen.; CNS-Gen.; Respiratory-Gen.; Vasotropic; Cerebroprotective; Neuroprotective; Nootropic; Antiparkinsonian; Anticonvulsant; Vulnerary; Hypnotic; Neuroleptic; Antidepressant; Gynecological; Tranquilizer; Analgesic; Eating-Disorders-Gen.; Antibacterial; Immunosuppressive; Dermatological; Virucide; Immunomodulator; Antipsoriatic.

MECHANISM OF ACTION - Inducible **nitric oxide** synthase inhibitor.

USE - For preparation of ionic salts from zwitterionic compounds e.g. S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine (claimed), which are useful in the treatment of disease e.g. cartilage degeneration in arthritis, rheumatoid arthritis, osteoarthritis, gouty arthritis, juvenile arthritis, septic arthritis, spondyloarthritis, acute rheumatic arthritis, enteropathic arthritis, neuropathic arthritis and pyogenic arthritis, chronic or inflammatory bowel disease, cardiovascular ischemia, diabetes, congestive heart failure, myocarditis, atherosclerosis, migraine, glaucoma, aortic aneurysm, reflux esophagitis, diarrhea, irritable bowel syndrome, cystic fibrosis, emphysema, asthma, bronchiectasis, hyperalgesia, cerebral ischemia, thrombotic stroke, global ischemia (secondary to cardiac arrest), multiple sclerosis and other central nervous system disorders mediated by NO (e.g. Parkinson's disease and Alzheimer's disease), neurodegenerative disorders, hypoxia, hypoglycemia, epilepsy, and in external wounds (such as spinal cord and head injury), hyperbaric oxygen convulsions' and toxicity, dementia e.g. pre-senile dementia, and AIDS-related dementia, Sydenham's chorea, Huntington's disease, Amyotrophic Lateral Sclerosis, Korsakoffs disease, imbecility relating to a cerebral vessel disorder, sleeping disorders, schizophrenia, depression, depression or other symptoms associated with Premenstrual Syndrome (PMS), anxiety and septic shock, pain, opiate tolerance in patients needing protracted opiate analgesics, and benzodiazepine tolerance in patients taking benzodiazepines, and other addictive behavior e.g. nicotine and eating disorders, systemic hypotension associated with septic and/or toxic shock, ocular conditions (such as ocular hypertension retinitis uveitis), systemic lupus erythematosus, glomerulonephritis, restenosis, inflammatory sequelae of viral infections, acute respiratory distress syndrome, oxidant-induced lung injury, IL2 therapy such as in a cancer patient, cachexia, immunosuppression such as in transplant therapy, disorders of gastrointestinal motility, sunburn, eczema, psoriasis, gingivitis, pancreatitis, damage to the gastrointestinal tract resulting from infections, adenomatous polyposis; for induction of labor, controlling tumor growth, chemotherapy; as antibacterial agents; as an adjuvant to short term immunosuppression in transplant therapy.

ADVANTAGE - The method does not require strong bases to remove cationic counterions, thus avoiding decomposition of the amidine functional group of salt compounds.

Dwg.0/5

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-L04; A12-M03; B10-A17; B14-A02; B14-C01; B14-C02; B14-C03; B14-C09; B14-D10; B14-E02; B14-E10; B14-E10A; B14-E10C; B14-F01; B14-F01G; B14-F02; B14-F02D; B14-F02D1; B14-F04; B14-F07; B14-F08; B14-J01; B14-J01A; B14-J01B1; B14-J01B3; B14-J07; B14-K01; B14-K01A; B14-N03; B14-N16; B14-N17; B14-S01; B14-S04; B14-S06

TECH UPTX: 20041019

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The salt compound is synthetic amino acid analog including amidine functional group (preferably S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine, dihydrochloride; S-(2-(ethanimidoylamino)-1-methylethyl)cysteine; (2S,5E)-2-amino-6-fluoro-7-)(1-iminoethyl)amino)-5-heptenoic acid, dihydrochloride; (S,E)-2-amino-2-methyl-6-((1-iminoethyl)amino)-4-hexenoic acid, dihydrochloride; (2S,5Z)-2-amino-2-methyl-7-((1-iminoethyl)amino)-5-heptenoic acid, dihydrochloride; or (2S,5E)-2-amino-2-methyl-6-fluoro-7-((1-iminoethyl)amino)-5-heptenoic acid, dihydrochloride). The cationic counterion is mineral acid and/or organic acid.

TECHNOLOGY FOCUS - POLYMERS - Preferred Method: The method is performed with ion exchange resin in a single stirred vessel or several batches in several vessels in series with intermediate filtering of the resin and replacement with fresh resin. The solution is passed through a resin bed contained within a column. Preferred Components: The ion exchange medium is anionic or cationic resin or ion exchange membrane.

ABEX UPTX: 20041019

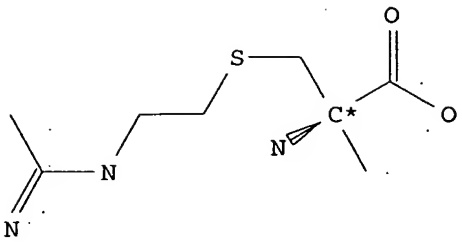
EXAMPLE - Amberlite IRA400 (RTM; strongly anionic quaternary ammonium polystyrene resin) (60 g) was pre-washed with ammonium hydroxide (4.7 weight%), followed by extensive washing with deionized water. A sample containing S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine dihydrochloride (0.9 g) in HCL/water (142 ml) was concentrated at 60degreesC, diluted to 60 ml with deionized water. Aliquots of the resin (0.5 g) were added to the solution. Total of 9 g resin was added. The final pH was 10.8. The resin was removed by filtration and the filtrate was concentrated at 60degreesC to form S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine. The final filtrate was assayed by HPLC and ion chromatography for chloride. The final chloride content was about 0.04 mol equivalents. HPLC assay showed no degradation of the sample.

DCSE 962301-1-3-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with GENERIC INORGANIC NEUTRAL COMPONENT
SDCN RAFIL7

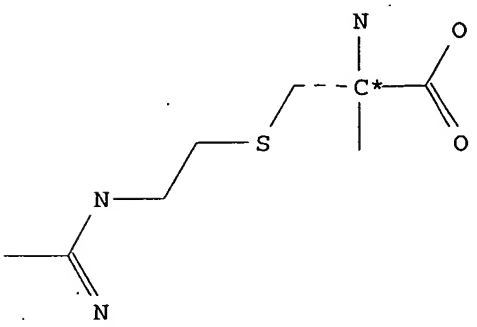
CM 1

Cl

CM 2



DCSE 465473-3-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8T



L66 ANSWER 16 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-677507 [66] WPIX
DOC. NO. CPI: C2004-241470
TITLE: New **crystalline** form (I) of S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine salicylate monohydrate is a **nitric oxide** synthase inhibitor useful to treat e.g. rheumatoid arthritis, inflammatory bowel disease, diabetes and atherosclerosis.
DERWENT CLASS: B05
INVENTOR(S): BROSTROM, L; BROSTROM, L R
PATENT ASSIGNEE(S): (BROS-I) BROSTROM L; (PHAA) PHARMACIA CORP
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004080953	A1	20040923	(200466)*	EN	46	C07C323-58
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
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US 2005239754	A1	20051027	(200571)			A61K031-60
EP 1603870	A1	20051214	(200582)	EN		C07C323-58

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
MC MK NL PL PT RO SE SI SK TR
MX 2005009779 A1 20051101 (200625) A61K031-155
BR 2004008182 A 20060321 (200629) C07C323-58

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
WO 2004080953	A1	WO 2004-IB645	20040304	
US 2005239754	A1 Provisional	US 2003-453772P	20030311	<--
		US 2004-797349	20040310	
EP 1603870	A1	EP 2004-717181	20040304	
		WO 2004-IB645	20040304	
MX 2005009779	A1	WO 2004-IB645	20040304	
		MX 2005-9779	20050912	
BR 2004008182	A	BR 2004-8182	20040304	
		WO 2004-IB645	20040304	

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1603870	A1 Based on	WO 2004080953
MX 2005009779	A1 Based on	WO 2004080953
BR 2004008182	A Based on	WO 2004080953

PRIORITY APPLN. INFO: **US 2003-453772P 20030311**; US 2004-797349 20040310

INT. PATENT CLASSIF.:
MAIN: A61K031-155; A61K031-60; C07C323-58
SECONDARY: A61P029-00

BASIC ABSTRACT:

WO2004080953 A UPAB: 20041015

NOVELTY - **Crystalline** S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine salicylate monohydrate (I) characterized by at least one of **x-ray powder pattern** having e.g. 1250 cm-1 at 11.5 degrees 2 theta), **Raman** spectrum having (e.g. 2050 cm-1 at 780 cps) and elemental **analysis** (e.g. in tetrahydrofuran the % of carbon, hydrogen, nitrogen, sulfur and water was 50.53, 7.23, 10.77, 7.96 and 0 respectively).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparation of (I).

ACTIVITY - Antiarthritic; Antirheumatic; Osteopathic; Antiinflammatory; Gastrointestinal-Gen.; Cardiovascular-Gen.; Vasotropic; Antidiabetic; Cardiant; Antiarteriosclerotic; Antimigraine; Ophthalmological; Antidiarrheic; CNS-Gen.; Respiratory-Gen.; Antiasthmatic.

MECHANISM OF ACTION - **Nitric oxide** synthase inhibitor.

No details of tests for **nitric oxide** synthase inhibitory activity are given.

USE - (I) is useful in the treatment of a condition where pathologically high production forms a part in a patient and also decreases **nitric oxide** production (claimed). (I) is also useful in inhibiting **nitric oxide** production from L-arginine that includes arthritic conditions e.g. rheumatoid arthritis, osteoarthritis, gouty arthritis and juvenile arthritis. (I) is also useful in the treatment of e.g. chronic or inflammatory bowel disease,

cardiovascular ischemia, diabetes, congestive heart failure, myocarditis, atherosclerosis, migraine, glaucoma, reflux esophagitis, diarrhea, irritable bowel syndrome, cystic fibrosis, emphysema and asthma.

ADVANTAGE - (I) has significantly less harmful side effects.

Dwg.0/12

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B10-B02D; B10-C03; B14-C01; B14-C02; B14-D03; B14-E02; B14-E10C; B14-F01B; B14-F01E; B14-F07; B14-K01; B14-N03; B14-S01; B14-S04

TECH UPTX: 20041015

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (claimed): Preparation of (I) comprises obtaining S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine zwitterion, adding S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine zwitterion to an appropriate solvent, adding a salicylic acid to the S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine and solvent and adding an antisolvent to precipitate S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine salicylate monohydrate **crystals.**

Preferred Process: In the preparation of (I) at least two solvents (N,N,dimethylformamide and water) are used. The antisolvent is acetonitrile.

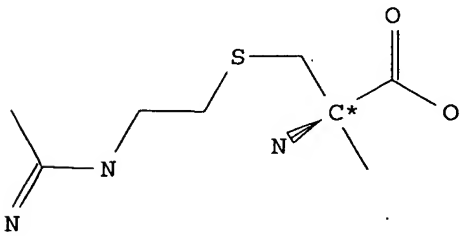
ABEX UPTX: 20041015

ADMINISTRATION - Administration of (I) is 0.01-100 (preferably 0.1-10) mg/kg for1-4 times/day, orally, intravascularly, intraperitoneally, subcutaneously, intramuscularly or topically.

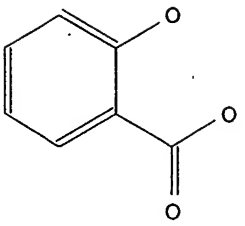
EXAMPLE - To a solution of S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine zwitterion (15 mg), salicylic acid (9.5 mg) in N,N-dimethyl formamide (250 microl) was added. Tetrahydrofuran (2.5 ml) was added drop wise with stirring and the solution developed a pearlescent precipitate. Inspection of the precipitate by polarized light microscopy showed birefringent acicular **crystals.** The precipitate was collected by filtration on a Millipore LS filter (5 microm pore size) and worked up to give **crystalline** form of S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine salicylate monohydrate.

DCSE 962365-1-1-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with 2-hydroxy-benzoic acid
SDCN RAFI57

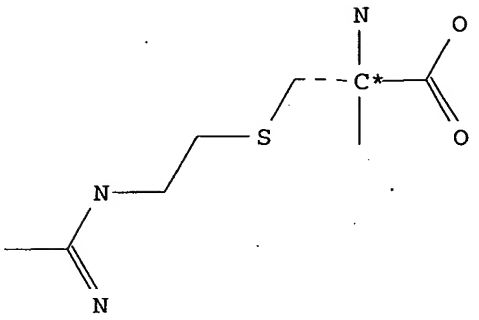
CM 1



CM 2



DCSE 465473-3-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8T



L66 ANSWER 17 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-561538 [54] WPIX
CROSS REFERENCE: 2004-553287 [53]
DOC. NO. CPI: C2004-205149
TITLE: Solid dispersion and non-hygroscopic pharmaceutical composition, useful to treat e.g. fever, comprises a hygroscopic and/or deliquescent drug dispersed or dissolved in a carrier medium comprising a matrix forming agent and a filler.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): GOKHALE, R D; TRIVEDI, J S
PATENT ASSIGNEE(S): (PHAA) PHARMACIA CORP; (GOKH-I) GOKHALE R D; (TRIV-I) TRIVEDI J S
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004060353	A1	20040722	(200454)*	EN	30	A61K009-16
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
AU 2003296948	A1	20040729	(200477)			A61K009-16
US 2005013856	A1	20050120	(200507)			A61K009-20
EP 1575564	A1	20050921	(200562)	EN		A61K009-16
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						

BR 2003017103	A	20051025 (200571)		A61K009-16
JP 2006514052	W	20060427 (200628)	21	A61K009-14

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE	
WO 2004060353	A1		WO 2003-US39510	20031211	<--
AU 2003296948	A1		AU 2003-296948	20031211	<--
US 2005013856	A1	Provisional	US 2002-435022P	20021219	<--
		Provisional	US 2002-435147P	20021219	<--
		Provisional	US 2002-435422P	20021219	<--
			US 2003-741526	20031218	<--
EP 1575564	A1		EP 2003-814729	20031211	<--
			WO 2003-US39510	20031211	<--
BR 2003017103	A		BR 2003-17103	20031211	<--
			WO 2003-US39510	20031211	<--
JP 2006514052	W		WO 2003-US39510	20031211	<--
			JP 2004-565403	20031211	<--

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003296948	A1	Based on	WO 2004060353
EP 1575564	A1	Based on	WO 2004060353
BR 2003017103	A	Based on	WO 2004060353
JP 2006514052	W	Based on	WO 2004060353

PRIORITY APPLN. INFO: **US 2002-435422P 20021219; US 2002-435022P 20021219; US 2002-435147P 20021219; US 2003-741526 20031218**

INT. PATENT CLASSIF.:

MAIN: A61K009-14; A61K009-16; A61K009-20

SECONDARY: A61K031-155; A61K031-185; A61K031-198; A61K031-465; A61K047-02; A61K047-04; A61K047-10; A61K047-12; A61K047-26; A61K047-32; A61K047-34; A61K047-36; A61K047-38; A61K047-40; A61P025-00; A61P025-04; A61P025-06; A61P025-34; A61P029-00; A61P029-02; A61P043-00

BASIC ABSTRACT:

WO2004060353 A UPAB: 20060502

NOVELTY - Solid dispersion and non-hygroscopic pharmaceutical composition (I) comprises a hygroscopic and/or deliquescent drug dispersed or dissolved in a carrier medium comprising a matrix forming agent and a filler.

DETAILED DESCRIPTION - Pharmaceutical composition (I) comprising a hygroscopic and/or deliquescent drug dispersed or dissolved in a carrier medium comprising a matrix forming agent (hydroxyethylcelluloses, hydroxypropylcelluloses, hydroxypropylmethylcelluloses, hydroxypropylmethylcellulose phthalates, polyvinylpyrrolidones, polyethylene glycols, polyglycolized glycerides, cyclodextrins and/or carbomers) and a filler, where (I) is a solid dispersion and is acceptably non-hygroscopic.

An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Antiinflammatory; Analgesic; Antismoking; Antipyretic.

MECHANISM OF ACTION - None given.

USE - Composition (I) is useful in the treatment of inflammation, pain, headache, smoking cessation or fever.

No biological data available.

ADVANTAGE - Composition (I) comprising the hygroscopic and/or deliquescent drug can be readily formulated into a convenient dosage forms. The solid dispersion has more resistance to **moisture absorption** and has better handling.

Dwg.0/2

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-V01; B04-C02A; B04-C02B; B04-C03; B05-A01B; B05-B02A3; B05-B02C; B07-A02B; B07-D03; B07-D04C; B10-A07; B10-A09A; B10-A17; B10-G02; B12-M05; B14-C01; B14-C03; B14-C04; B14-D10; B14-M01B

TECH UPTX: 20040823

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation (claimed): Composition (I) is prepared by:

(1) dissolving the hygroscopic and/or deliquescent drug, the filler and the matrix forming agent (hydroxypropylcellulose, hydroxypropylmethycellulose, hydroxypropylmethylcellulosephthalate, polyvinylpyrrolidone, polyethylene glycol, polyglycolized glycerides and/or cyclodextrins) in a solvent, in any order or simultaneously and removing the solvent using elevated temperature or a vacuum or by freeze drying or spray drying to form a solid dispersion of the drug in a carrier medium comprising the filler and the matrix forming agent; or by heating a matrix forming agent temperature above its **melting** point, adding the filler and the hygroscopic and/or deliquescent drug, in any order or, simultaneously, to the resulting **melted** matrix forming agent with mixing to form a composite and cooling the composite with mixing to form a solid dispersion of the drug in the carrier medium comprising the filler and the matrix forming agent.

Preferred Process: Composition (I) is formed by a solvent method, a fusion method or a fusion-solvent method.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The drug has a hygroscopicity and when unformulated it exhibits at least about 15% mass increase at equilibrium when exposed to 60% relative humidity at 21-23 degrees C. (I) exhibits an equilibrium mass increase of less than about 10% when exposed to 60% relative humidity at 21-23 degrees C.

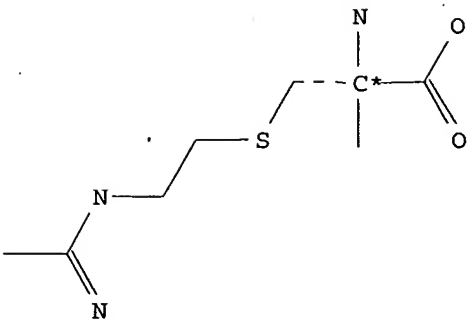
The drug (about 1-75 wt% of (I)) is an iNOS (**nitric oxide** synthase) inhibitor, nicotine or S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine and/or their pharmaceutically acceptable salt.

The filler (1-95 wt% of (I)) (preferably tribasic calcium phosphates, anhydrous calcium sulfates, carboxymethylcellulose calciums, carboxymethylcellulose sodiums, anhydrous dextroses, fructoses, anhydrous lactoses, anhydrous magnesium stearates, magnesium trisilicates, maltodextrins, methylcelluloses, **microcrystalline** celluloses, powdered celluloses, pregelatinized starchs, starchs, sterilizable maize starchs, compressible sugars or confectioner's sugars) is hygroscopic and/or deliquescent **microcrystalline** cellulose and it enables the solid dispersion to be flowable. The polyethylene glycol has an average molecular weight of about 1,000-35,000 daltons. (I) is in a form suitable for oral administration (preferably in the form of a tablet).

ABEX UPTX: 20040823

ADMINISTRATION - Administration of (I) is oral (claimed), buccal, sublingual, topical or rectal. No dosage given.

DCSE 465473-3-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8T



L66 ANSWER 18 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-553287 [53] WPIX
CROSS REFERENCE: 2004-561538 [54]
DOC. NO. CPI: C2004-202449
TITLE: Solid particulate composition, useful to provide a hygroscopic and/or deliquescent drug in a non-hygroscopic formulation to treat e.g. pain, comprises a hygroscopic and/or deliquescent drug and at least one non-hygroscopic polymer.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): CZYZEWSKI, A M; GAO, D; GOKHALE, R D; TRIVEDI, J S
PATENT ASSIGNEE(S): (CZYZ-I) CZYZEWSKI A M; (GAOD-I) GAO D; (PHAA) PHARMACIA CORP
COUNTRY COUNT: 109
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004060352	A1	20040722	(200453)*	EN	30	A61K009-16
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW						
US 2004197411	A1	20041007	(200466)			A61K009-14
AU 2003298010	A1	20040729	(200477)			A61K009-16
NL 1025069	C2	20050216	(200525)			A61K047-38
EP 1575563	A1	20050921	(200562)	EN		A61K009-16
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
TW 2004013006	A	20040801	(200581)			A61K047-30
BR 2003017392	A	20051220	(200604)			A61K009-16
TW 2004023971	A	20041116	(200609)			A61K009-16
MX 2005006802	A1	20050901	(200617)			A61K031-155
JP 2006513238	W	20060420	(200627)		22	A61K009-16

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
WO 2004060352	A1	WO 2003-US38792	20031205	<--
US 2004197411	A1 Provisional	US 2002-435022P	20021219	<--

		Provisional	US 2002-435147P	20021219	<--
		Provisional	US 2002-435422P	20021219	<--
			US 2003-741530	20031218	<--
AU 2003298010	A1		AU 2003-298010	20031205	<--
NL 1025069	C2		NL 2003-1025069	20031218	<--
EP 1575563	A1		EP 2003-796731	20031205	<--
			WO 2003-US38792	20031205	<--
TW 2004013006	A		TW 2003-135960	20031218	<--
BR 2003017392	A		BR 2003-17392	20031205	<--
			WO 2003-US38792	20031205	<--
TW 2004023971	A		TW 2003-135756	20031217	<--
MX 2005006802	A1		WO 2003-US38792	20031205	<--
			MX 2005-6802	20050620	
JP 2006513238	W		WO 2003-US38792	20031205	<--
			JP 2004-565235	20031205	<--

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003298010	A1	Based on	WO 2004060352
EP 1575563	A1	Based on	WO 2004060352
BR 2003017392	A	Based on	WO 2004060352
MX 2005006802	A1	Based on	WO 2004060352
JP 2006513238	W	Based on	WO 2004060352

PRIORITY APPLN. INFO: **US 2002-435422P 20021219; US 2002-435022P 20021219; US 2002-435147P 20021219; US 2003-741530 20031218**

INT. PATENT CLASSIF.:

MAIN: A61K009-14; A61K009-16; A61K031-155; A61K047-30; A61K047-38

SECONDARY: A61K031-185; A61K031-198; A61K047-02; A61K047-04; A61K047-26; A61K047-36; A61P001-00; A61P001-02; A61P001-04; A61P001-16; A61P001-18; A61P003-00; A61P003-10; A61P005-00; A61P005-14; A61P007-00; A61P007-06; A61P009-00; A61P009-10; A61P011-00; A61P011-06; A61P011-08; A61P015-00; A61P015-06; A61P015-08; A61P017-00; A61P017-02; A61P017-06; A61P019-00; A61P019-02; A61P019-06; A61P021-00; A61P021-04; A61P025-00; A61P025-06; A61P025-28; A61P027-00; A61P027-02; A61P027-06; A61P027-12; A61P027-16; A61P029-00; A61P035-00; A61P037-00; A61P037-02; A61P037-08; A61P043-00

BASIC ABSTRACT:

WO2004060352 A UPAB: 20060426

NOVELTY - Solid particulate composition (I) comprises a (hygroscopic and/or deliquescent) drug (A) and at least one non-hygroscopic polymer (B) in intimate association. The composition is acceptably non-hygroscopic.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a preparation of (I).

ACTIVITY - Antiinflammatory; Antiarthritic; Analgesic; Antipyretic.

MECHANISM OF ACTION - Inducible **nitric oxide** synthase inhibitor.

USE - Composition (I) is useful to provide hygroscopic and/or deliquescent drugs in a pharmaceutically acceptable, non-hygroscopic formulation for the treatment of e.g. inflammation, arthritis and

nitric oxide synthase-mediated disorders such as pain, headaches or fever.

No biological data available.

ADVANTAGE - Composition (I) is acceptably non-hygroscopic that does not **absorb** substantial amounts of **moisture** when subjected to relatively humid conditions. The shelf life, flow, handling and processing properties of (I) are generally not substantially affected by exposure to moisture conditions. The hygroscopic and/or deliquescent drugs are prepared into acceptably non-hygroscopic formulation intermediates using the aqueous spray drying process. Spray drying using an aqueous dispersion avoids potential chemical interaction between a non-aqueous solvent and drug, and eliminates potential toxicities associated with many non-aqueous solvents.

Dwg.0/5

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: A12-V01; B04-C02A; B04-C02B; B05-A01B; B05-B02A3; B05-B02C; B07-A02B; B10-A07; B10-A17; B10-G02; B12-M05; B12-M06; B14-C01; B14-C03; B14-C04; B14-C09; B14-D10

TECH UPTX: 20040818

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preparation (claimed): Preparation of (I) comprises dispersion of a hygroscopic and/or deliquescent drug and at least one non-hygroscopic polymer in an aqueous liquid to form a dispersion and removal of the aqueous liquid from the dispersion.

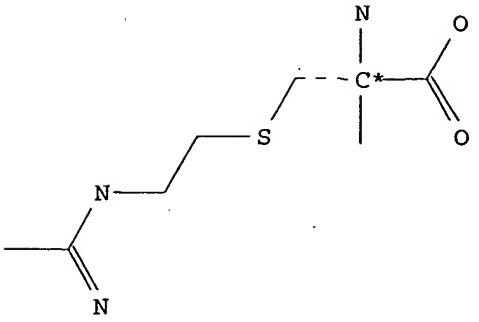
Preferred Process: The step of removing the aqueous liquid from the dispersion comprises spray drying, lyophilizing, elevating temperature and/or vacuum filtrating.

Preferred Composition: Active agent (A) is an inducible **nitric oxide** synthase inhibitor (preferably S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine or its salt). (I) exhibits a mass increase of not more than 10% when exposed to 40% relative humidity at 21-23degreesC for a period of 24 hours or for a period of time sufficient for (I) to reach equilibrium.

Polymer (B) is a cellulosic polymer (preferably hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose or ethylcellulose). (B) (10-80 wt%) and (A) (10-85 wt%) are present in a weight ratio of 1:2-2:1. (B) exhibits a moisture content of not more than 6% at 40% relative humidity and 21-23degreesC.

Composition (I) further comprises a (hygroscopic and/or deliquescent) filler (preferably tribasic calcium phosphate, anhydrous calcium sulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, anhydrous dextrose, fructose, anhydrous lactose, anhydrous magnesium stearate, magnesium trisilicate, maltodextrin, methylcellulose, **microcrystalline** cellulose, powdered cellulose, pregelatinized starch, starch, sterilizable maize starch, compressible sugar or a confectioner's sugar). (I) is in the form of a flowable and/or compressible powder.

DCSE 465473-3-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8T



L66 ANSWER 19 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-090631 [09] WPIX
DOC. NO. CPI: C2004-036762
TITLE: Treating respiratory disease or condition e.g. allergic induced asthma, acute mountain sickness and hypoxia comprises involves use of inducible **nitric oxide** synthase inhibitors.
DERWENT CLASS: B05
INVENTOR(S): MANNING, P T
PATENT ASSIGNEE(S): (MANN-I) MANNING P T; (PHAA) PHARMACIA CORP
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003097163	A2	20031127	(200409)*	EN	111	A61P011-00<--
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW						
US 2004077639	A1	20040422	(200428)			A61K031-54
AU 2003234606	A1	20031202	(200442)			A61P011-00<--
EP 1506040	A2	20050216	(200513)	EN		A61P011-00
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR						
BR 2003011180	A	20050301	(200519)			A61P011-00
KR 2005004155	A	20050112	(200535)			A61K031-198
MX 2004011404	A1	20050301	(200568)			A61K031-198
CN 1652843	A	20050810	(200572)			A61P011-00
JP 2005536467	W	20051202	(200582)		161	A61K031-198

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE	
WO 2003097163	A2		WO 2003-US15369	20030516	<--
US 2004077639	A1	Provisional	US 2002-381054P	20020516	<--
			US 2003-439669	20030516	<--
AU 2003234606	A1		AU 2003-234606	20030516	<--
EP 1506040	A2		EP 2003-728948	20030516	<--
			WO 2003-US15369	20030516	<--
BR 2003011180	A		BR 2003-11180	20030516	<--
			WO 2003-US15369	20030516	<--

KR 2005004155	A	KR 2004-718523	20041116	
MX 2004011404	A1	WO 2003-US15369	20030516	<--
		MX 2004-11404	20041116	
CN 1652843	A	CN 2003-811196	20030516	<--
JP 2005536467	W	WO 2003-US15369	20030516	<--
		JP 2004-505156	20030516	<--

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003234606	A1 Based on	WO 2003097163
EP 1506040	A2 Based on	WO 2003097163
BR 2003011180	A Based on	WO 2003097163
MX 2004011404	A1 Based on	WO 2003097163
JP 2005536467	W Based on	WO 2003097163

PRIORITY APPLN. INFO: **US 2002-381054P 20020516; US 2003-439669 20030516**

INT. PATENT CLASSIF.:

MAIN: A61K031-198; A61K031-54; A61P011-00

SECONDARY: A61K031-16; A61K031-22; A61K031-401; A61K031-41; A61K031-421; A61K031-426; A61K031-4439; A61K031-445; A61K031-495; A61K031-537; A61K031-55; A61P007-02; A61P009-12; A61P011-06; A61P011-08; A61P031-04; A61P037-08; A61P043-00

BASIC ABSTRACT:

WO2003097163 A UPAB: 20040205

NOVELTY - Treatment of respiratory disease or condition involves administering inducible **nitric oxide** synthase inhibitors.

DETAILED DESCRIPTION - Treating respiratory disease or condition comprises administering an inducible **nitric oxide** synthase inhibitor which comprises H3C-C(=NR7)-HN-CH2-C(R1)=C(R2)-CH2-CH2-CHNH2-C(O)-J (I), R21-N=C(R23)-NR22-C(R19)(R20)-C(R11)(R17)-X-C(R15)(R16)-C(R12)(NR13R14)-C(O)R18 (II), H3C-C(=NH)-NH-CH2-C(R41)=C(R42)-(CH2)2-CHNH2-CO2H (III), a compound of formula (IV), H3C-C(=NH)-NH-CH2-C(R41)=C(R44)-CH2-C(R45)(NH2)-CO2H (V), H3C-C(=NH)-NH-C equivalent to CH2-C(H2N)(R46)(CO2H) (VI), H3C-C(=NH)-NH-CH2-CH2-C(R47)=C(R48)-CH2-C(R49)(NH2)(CO2H) (VII), H3C-C(=NH)-NH-CH2-CH2-C equivalent to CH2-C(NH2)(R50)-CO2H (VIII), H3C-C(=NH)-NH-CH2-C(R50a)=C(R51)-C(R53)(R54)-CH2-C(R52)(NH2)(CO2H) (IX), H3C-C(=NH)-NH-C equivalent to C-CH2-CH2-C(R55)(NH2)(CO2H) (X), 2S-amino-6-((1-iminoethyl)amino)-N-(1H-tetrazol-5-yl)hexanamide (XI), hydrate, dihydrochloride, H2N-CHCH3-N-CH2-CH(R79)-S-CH2-CHNH2-CO2H (XII), a compound of formula (XIII), (XIV) or (XV), PPA250 (RTM; 3-(2,4-difluorophenyl)-6-(2-(4-(1H-imidazol-1-ylmethyl)phenoxy)ethoxy)-2-phenylpyridine), their salts or prodrugs.

R1, R2, R43, R44, R47, R48 = H , halo or optionally substituted alkyl;

R7 = H or OH;

J = OH, alkoxy or optionally substituted amino;

R12 = e.g. 1-6C alkyl, 2-6C alkenylor 2-6C alkynyl (all optionally substituted);

R18 = OR24 or optionally substituted amino;

R13, R21, R22 = e.g. H or OH;

R14 = e.g. H;

R11, R15, R16, R17 = H, halo, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-5C alkoxy(1C)alkyl;

R19, R20 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-5C alkoxy(iC)alkyl;
R23 = 1C alkyl;
R24 = e.g. H or optionally substituted 1-6C alkyl;
X = S, S(O) or S(O)2;
R41, R42 = H or methyl;
R45, R49 = 1-5C alkyl (optionally substituted by alkoxy or at least one halo);
R46, R50, R52, R55 = 1-5C alkyl (optionally substituted by halo or alkoxy (optionally substituted by at least one halo));
R50a, R51, R53 = H, halo or 1-5C alkyl (optionally substituted by halo or alkoxy (optionally substituted by at least one halo);
R54 = halo or 1-5C alkyl (optionally substituted by halo or alkoxy (optionally substituted by at least one halo));
R79 = 1-4C alkyl, 3-4C cycloalkyl, 1-4C hydroxyalkyl or 1-4C haloalkyl;
A = e.g. R56;
X, Y', Z, U' = e.g. N;
V' = e.g. S or O;
W' = N or CH;
Q = e.g. a direct bond or C(O);
m = 0-4;
n = 0-3;
q, r = 0 or 1;
t = 0-2;
Q2 = optionally substituted N-heterocyclyl;
D = carbocyclyl or heterocyclyl (both optionally substituted);
R56 = e.g. 1-20C alkyl or cycloalkyl;
R58 = e.g. H, alkyl or cycloalkyl;
R67-R70, R72, R75 = H or alkyl.
Full Definitions are given in the DEFINITIONS (Full definitions) section.

ACTIVITY - Antiasthmatic; Respiratory-Gen.; CNS Gen.; Antiinflammatory; Hypotensive; Immunosuppressive; Antibacterial.

MECHANISM OF ACTION - Inducible nitric oxide synthase inhibitor.

A human cartilage explants assay was carried out by rinsing bone pieces twice with Dulbecco's phosphate buffered saline and once with Dulbecco's Modified Eagles Medium and placed into a petri dish with phenol red free minimum essential medium. Cartilage was cut into small explants (15-45 mg) and one or two explants per well were placed into either 96 or 48 well culture plates with culture media (200-500 mu l) per well. The culture media included either a custom modification of minimum essential medium with Earle's salts prepared without L-arginine, without L-glutamine and without phenol red or a custom modification of serumless Neuman and Tytell medium prepared without L-arginine without insulin, without ascorbic acid, without L-glutamine and without phenol red. Both were supplemented before use with L-arginine (100 mu M), L-glutamine (2 mM), 1 multiply HL-1 supplement, ascorbic acid (50 mg/ml) and recombinant human interleukin 1(150 pg/ml) to induce nitric oxide synthase.

(2S,5E)-2-Amino-6-fluoro-7-((1-iminoethyl)amino)-5-heptanoic acid, dihydrochloride, monohydrate (Ia) was then added in 10 mu l aliquots and the explants incubated at 37 deg. C with 5% CO2 for 18-24 hours. IC50 value of (Ia) was 0.1 mu M.

USE - Used for treating respiratory diseases or conditions e.g. asthmatic condition, chronic obstructive pulmonary disease, allergic-induced asthma, exercise induced asthma, pollution-induced asthma, cold-induced asthma, viral-induced asthma, chronic bronchitis with normal airflow, chronic obstructive bronchitis, emphysema, asthmatic bronchitis, bullous disease, cystic fibrosis, pigeon fancier's disease, farmer's lung, acute respiratory distress syndrome, pneumonia, aspiration

or inhalation injury, fat embolism in the lung, acidosis inflammation of the lung, acute pulmonary edema, acute mountain sickness, post-cardiac surgery, acute pulmonary hypertension, persistent pulmonary hypertension of the newborn, perinatal aspiration syndrome, hyaline membrane disease, acute pulmonary thromboembolism, heparin-protamine reactions, sepsis, status asthmaticus and hypoxia (all claimed).

ADVANTAGE - The method provides overall treatment efficacy with minimal toxicity and adverse side effects.

Dwg.0/4

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B07-H04; B10-A10; B10-A17; B14-C03; B14-F02B; B14-K01A; B14-K01D; B14-K01F; B14-S06
ABEX UPTX: 20040205

SPECIFIC COMPOUNDS - 48 Specific compounds are preferably used e.g. (2S,5E)-2-amino-6-fluoro-7-((1-iminoethyl)amino)-5-heptanoic acid, dihydrochloride, monohydrate (Ia).

ADMINISTRATION - The dosage is 0.001-2500 mg/kg/day by inhalation (e.g. oral or nasal inhalation), orally, intravenously, subcutaneously, rectally, topically, buccally (e.g. sublingually), intramuscularly or intradermally.

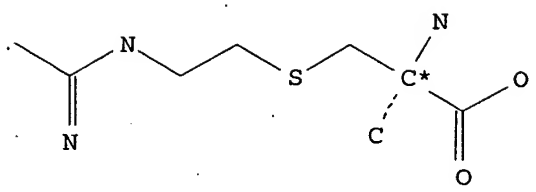
EXAMPLE - No relevant example is given.

DEFINITIONS - Full Definitions:

R1, R2 = H, halo or alkyl (optionally substituted by at least one halo);
R7 = H or OH;
J = OH, alkoxy or NR3R4;
R3 = H, lower alkyl, lower alkylenyl or lower alkynyl;
R4 = H or heterocyclyl containing 1-4 O, S or N heteroatoms (optionally substituted by heteroarylamino, N-aryl-N-alkylamino, N-heteroarylamino-N-alkylamino, haloalkylthio, alkanoyloxy, alkoxy, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, OH, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkylamidosulfonyl, dialkylamidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydroxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, cyanoalkyl, dicyanoalkyl, carboxamidoalkyl, dicarboamidoalkyl, cyanocarboalkoxyalkyl, carboalkoxyalkyl, dicarboalkoxyalkyl, cyanocycloalkyl, dicyanocycloalkyl, carboxamidocycloalkyl, dicarboxamidocycloalkyl, carboalkoxycyanocycloalkyl, carboalkoxycycloalkyl, dicarboalkoxycycloalkyl, formylalkyl, acylalkyl, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, phosphonoalkyl, dialkoxyphosphonoalkoxy, diaralkoxyphosphonoalkoxy, phosphonoalkoxy, dialkoxyphosphonoalkylamino, diaralkoxyphosphonoalkylamino, phosphonoalkylamino, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, guanidino, amidino or acylamino);
X = S, SO or SO2;
R12 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-5C alkoxy(1C)alkyl or 1-5C alkylthio(1C)alkyl (all optionally substituted by at least one OH, alkoxy

or halo);
R18 = OR24, N(R25)(R26), N(R30) or O;
R13 = H, OH, C(O)R27, C(O)OR28, C(O)SR29, C(O) or C(R31)(R32);
R14 = C(O)OR33 or H;
R11, R15, R16, R17 = H, halo, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-5C alkoxy(1C)alkyl;
R19, R20 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-5C alkoxy(1C)alkyl;
R21 = H, OH, C(O)OR34, C(O)SR35, O or C(O);
R22 = H, OH, C(O)OR36, C(O)SR37, O or C(O), or
R18 + R13, R21 + R22 = a ring;
R23 = 1C alkyl;
R24 = H or 1-6C alkyl (optionally substituted by Q1);
R25 = alkyl or alkoxy (both optionally substituted by Q1) or H;
R26 = alkyl or alkoxy (both optionally substituted by Q1), H, OH, C(O)R38, C(O)OR39, C(O)SR40 or Q1;
Q1 = cycloalkyl, heterocyclyl, aryl or heteroaryl;
R27-R40 = H or alkyl (optionally substituted by at least one Q1);
R41, R42 = H or methyl;
R43, R44, R47, R48 = H, halo or 1-5C alkyl (optionally substituted by alkoxy or at least one halo);
R45, R49 = 1-5C alkyl (optionally substituted by alkoxy or at least one halo);
R46, R50, R52, R55 = 1-5C alkyl (optionally substituted by halo or alkoxy (optionally substituted by at least one halo));
R50a, R51, R53 = H, halo or 1-5C alkyl (optionally substituted by halo or alkoxy (optionally substituted by at least one halo));
R54 = halo or 1-5C alkyl (optionally substituted by halo or alkoxy (optionally substituted by at least one halo));
R79 = 1-4C alkyl, 3-4C cycloalkyl, 1-4C hydroxyalkyl or 1-4C haloalkyl;
A = R56, OR56, C(O)N(R56)(R57), P(O)(N(R56)R57)2, N(R56)C(O)R57, N(R76)C(O)OR56, N(R56)R76, N(R71)C(O)N(R56)R71, S(O)tR56, SO2R56, SO2NHC(O)R56, NHSO2R77, SO2NH(R56)H, C(O)NHSO2R77 or CH=NOR56;
X, Y', Z = N or C(R19);
U' = N or C(R60);
V' = N(R59), S, O or C(R59)H;
W' = N or CH;
Q = C(O), O, C(=NR56), S(O)t, N(R61), heteroatom, N(R58) or a direct bond to R58;
m = 0-4;
n = 0-3;
q, r = 0 or 1;
t = 0-2;
Q2 = optionally substituted N-heterocyclyl;
D = carbocyclyl or heterocyclyl (both optionally substituted);
R56, R57 = 1-20C alkyl, cycloalkyl or heterocyclyl (all optionally substituted), (0-8C alkyl)-R64, (2-8C alkenyl)-R64, (2-8C alkynyl)-R64, (2-8C alkyl)-R65 or (1-8C)-R66 (both optionally substituted by OH) or H, or
NR56R57 = optionally substituted N-heterocyclyl;
R58 = H, alkyl, cycloalkyl, optionally substituted aryl, haloalkyl, (1-8C alkyl)-C(O)N(R56)R57, (1-8C alkyl)-N(R56)R57, (1-8C alkyl)-R63, (2-8C alkyl)-R65, (1-8C alkyl)-R66 or heterocyclyl (optionally substituted by at least one halo, alkyl, alkoxy or imidazolyl), or
QR58 = COOH, C(O)N(R56)R57 or pyrrolidine-2,5-dion-1-yl (substituted at positions 3 and 4 by R57 and R56, respectively);
R59 = aryl or aralkyl (both optionally substituted), H, alkyl or cycloalkyl;
R60 = H, alkyl, aryl, aralkyl, haloalkyl, OR71, S(O)tR71, N(R71)R76, N(R71)C(O)N(R56)R71, N(R71)C(O)OR71, N(R71)C(O)R71, (0-8C

alkyl)-C(H)(C(O)R71)2 or (0-8C alkyl)-C(O)N(R56)R71;
R61 = aryloxycarbonyl, aralkoxycarbonyl, aryl, heterocyclyl, arylsulfonyl, arylaminocarbonyl or N-heterocyclyl (all optionally substituted), H, alkyl, cycloalkyl, (1-8C alkyl)-R63, (2-8C alkyl)-R65, (1-8C alkyl)-R66, acyl, C(O)R63, C(O)(1-6C alkyl)-R63, alkoxycarbonyl, alkylsulfonyl, alkoxycarbonylalkyl, carboxyalkyl, aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, aminosulfonyl, monoalkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, arylsulfonylaminocarbonyl, C(=NH)-N(CN)R56, C(O)R78N(R56)R57, C(O)N(R56)R78C(O)OR56;
R63, R64 = haloalkyl, cycloalkyl (optionally substituted by halo, cyano, alkyl or alkoxy), carbocyclyl (optionally substituted by halo, alkyl or alkoxy) or heterocyclyl (optionally substituted by alkyl, aralkyl or alkoxy);
R65 = aryloxy, aralkoxy or S(O)tR77 (all optionally substituted), halo, alkoxy, acylamino, amino, monoalkylamino, dialkylamino, (triphenylmethyl)amino, hydroxy, mercapto or alkylsulfonamido;
R66 = cyano, di(alkoxy)alkyl, carboxy, alkoxycarbonyl, aminocarbonyl, monoalkylaminocarbonyl or dialkylaminocarbonyl;
R67-R70, R72, R75 = H or alkyl;
R71 = aryl or aralkyl (both optionally substituted), H, alkyl or cycloalkyl;
R73 = H, NO2 or toluenesulfonyl;
R74 = H, alkyl (optionally substituted by OH), cyclopropyl, halo or haloalkyl;
R76 = aryl or aralkyl (both optionally substituted), H, alkyl, cycloalkyl, C(O)R77 or SO2R77, or
NR76R56, NR7671 = optionally substituted N-heterocyclyl;
R77 = aryl or aralkyl (both optionally substituted), alkyl or cycloalkyl, and
R78 = amino acid residue,
provided that:
(1) at least one of R1 and R2 contains a halo;
(2) when R18 is OR24 or N(R25)(R26), then R13 is H, OH, C(O)R27, C(O)OR28 or C(O)SR29, when R18 is N(R30), then R13 is C(O), and when R18 is O, then R13 is C(R31)(R32);
(3) when R13 is C(R31)(R32), then R14 is C(O)OR33;
(4) when R21 is O, then R22 is C(O), and when R21 is C(O), then R22 is O;
(5) when R25 is H, then R26 is Q1;
(6) the alkyl, alkenyl, alkynyl, alkoxy, alkylthio and Q1 of R11-R40 are optionally substituted by at least one of OH, alkoxy or halo;
(7) U' is N only when X' is N and Z and Y' are CR74;
(8) when Q and V' are heteroatoms, m, q and r cannot all be 0;
(9) when A is OR56, N(R56)C(O)R57, N(R71)C(O)OR57, N(R56)R76, N(R71)C(O)N(R56)R71, S(O)tR56 (where t is 0) or NHSO2R77, n, q and r cannot all be 0; and when Q is a heteroatom and A is OR56, N(R56)C(O)R57, N(R71)C(O)OR57, N(R56)R76, N(R71)C(O)N(R56)R71, S(O)tR56 (where t is 0) or NHSO2R77, m and n cannot both be 0;
(10) when Q is N(R58) or a direct bond to R58, then R58 is additionally aminocarbonyl, alkoxycarbonyl, alkylsulfonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl or C(=NR73)-NH2, and
(11) when A is R56 or OR56, R59 cannot be hydrogen and when V is CH, R59 may additionally be OH.
DCSE 465473-1-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5HUE

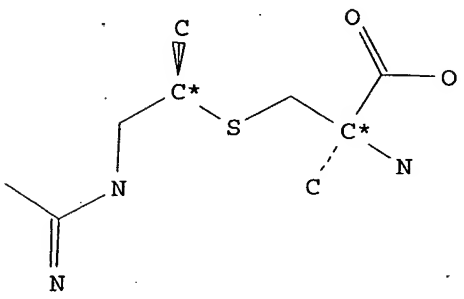


DCSE 478285-4-2-0
CN.S 3-(2-Acetimidoylamino-1-methyl-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with GENERIC INORGANIC NEUTRAL COMPONENT
SDCN RACSJE

CM 1

Cl

CM 2

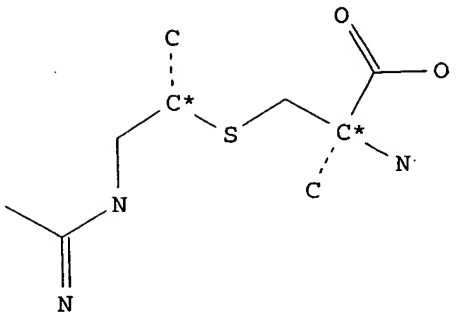


DCSE 478285-3-1-0
CN.S 3-(2-Acetimidoylamino-1-methyl-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with GENERIC INORGANIC NEUTRAL COMPONENT
SDCN RACSJG

CM 1

Cl

CM 2

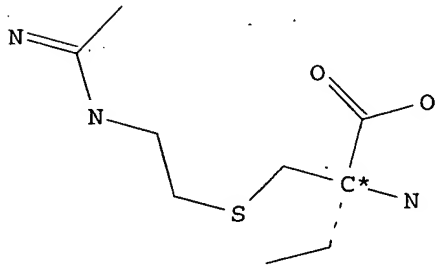


DCSE 478290-2-1-0
CN.S 2-(2-Acetimidoylamino-ethylsulfanylmethyl)-2-amino-butyric acid; compound with GENERIC INORGANIC NEUTRAL COMPONENT
SDCN RACSJJ

CM 1

Cl

CM 2

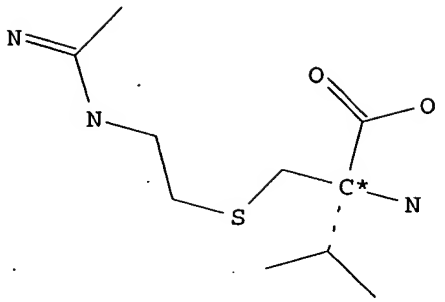


DCSE 478296-2-1-0
CN.S 2-(2-Acetimidoylamino-ethylsulfanylmethyl)-2-amino-3-methyl-butyric acid; compound with GENERIC INORGANIC NEUTRAL COMPONENT
SDCN RACSJL

CM 1

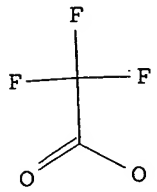
Cl

CM 2

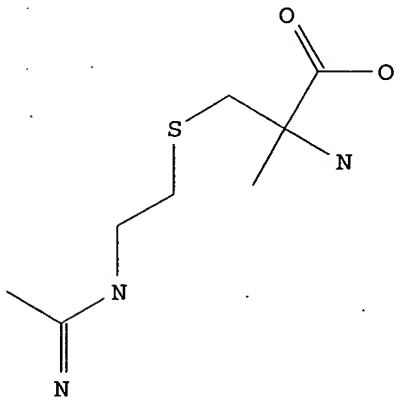


DCSE 831193-0-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid; compound with trifluoro-acetic acid
SDCN RACSJU

CM 1



CM 2

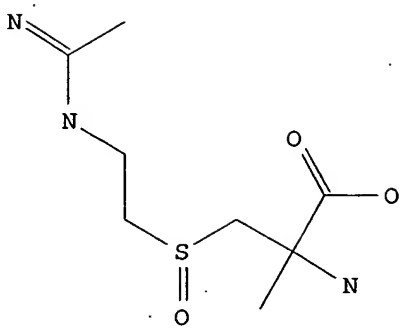


DCSE 478305-0-1-0
CN.S 3-(2-Acetimidoylamino-ethanesulfinyl)-2-amino-2-methyl-propionic acid; hydrochloride
SDCN RACSJW

CM 1

Cl

CM 2

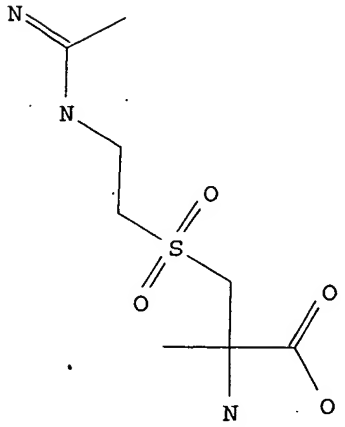


DCSE 478306-0-1-0
CN.S 3-(2-Acetimidoylamino-ethanesulfonyl)-2-amino-2-methyl-propionic acid; hydrochloride
SDCN RACSJY

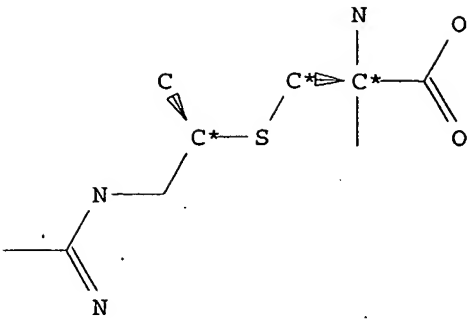
CM 1

Cl

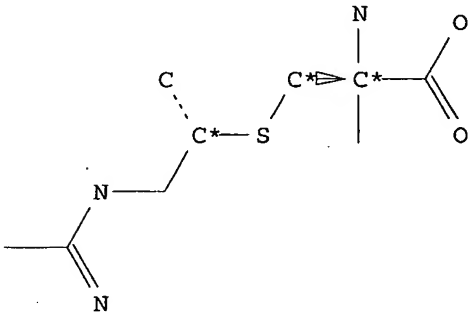
CM 2



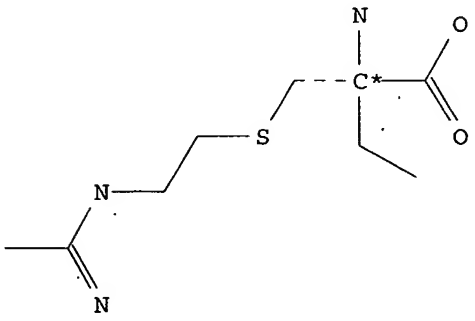
DCSE 478285-2-0-0
CN.S 3-(2-Acetimidoylamino-1-methyl-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8X



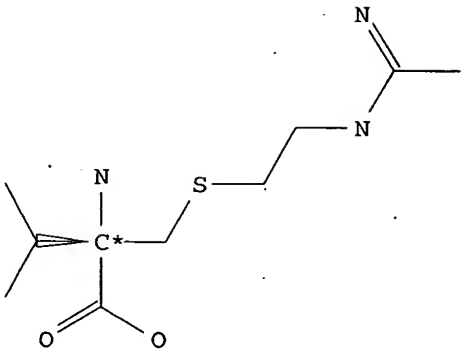
DCSE 478285-1-0-0
CN.S 3-(2-Acetimidoylamino-1-methyl-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8W



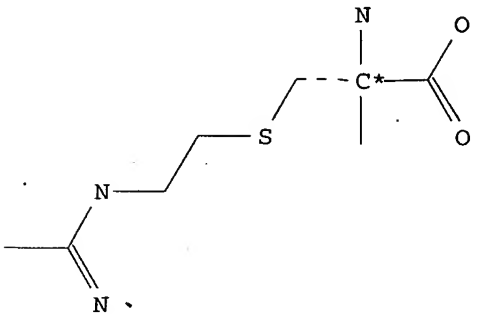
DCSE 478290-1-0-0
CN.S 2-(2-Acetimidoylamino-ethylsulfanylmethyl)-2-amino-butyric acid
SDCN RA5R91



DCSE 478296-1-0-0
CN.S 2-(2-Acetimidoylamino-ethylsulfanylmethyl)-2-amino-3-methyl-butyric acid
SDCN RA5R97



DCSE 465473-3-0-0
CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid
SDCN RA5R8T



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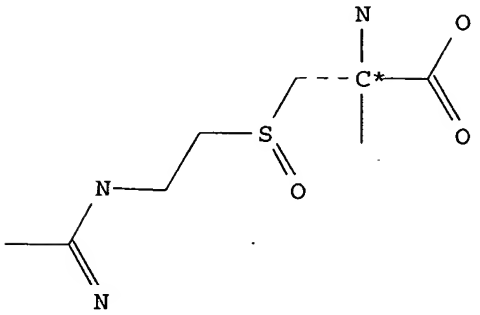
CN.S 3-(2-Acetimidoylamino-ethanesulfinyl)-2-amino-2-methyl-propionic acid
SDCN RA5R9G



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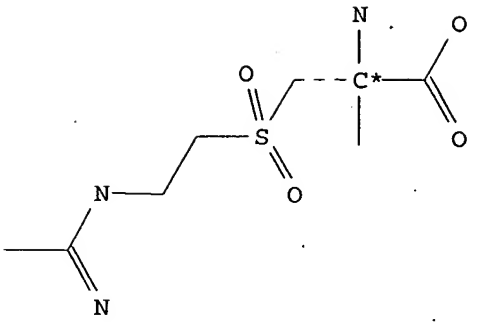
CN.S 3-(2-Acetimidoylamino-ethanesulfonyl)-2-amino-2-methyl-propionic acid
SDCN RA5R9H



L66 ANSWER 20 OF 20 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-103206 [09] WPIX
DOC. NO. CPI: C2003-025936
TITLE: Composition for treating cancer e.g. of bladder, pancreas, ovary and prostate, comprises a selective inhibitor for inducible **nitric oxide** synthase and a cyclooxygenase-2 inhibitor.
DERWENT CLASS: B02 B05
INVENTOR(S): CONNOR, J R; MANNING, P T; RAO, C V; REDDY, B S; SEIBERT, K
PATENT ASSIGNEE(S): (CONN-I) CONNOR J R; (MANN-I) MANNING P T; (RAOC-I) RAO C V; (REDD-I) REDDY B S; (SEIB-I) SEIBERT K; (PHAA) PHARMACIA CORP
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
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RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW						
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US 2003013702	A1	20030116	(200313)			A61K031-66<--
AU 2002248693	A1	20021008	(200432)			A61K000-00<--
EP 1463495	A2	20041006	(200465)	EN		A61K031-16
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR						
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MX 2003008582	A1	20040101	(200471)			A61K000-00000
JP 2005500259	W	20050106	(200505)		476	A61K031-198
US 7012098	B2	20060314	(200620)			A61K031-185

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
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		US 2001-961969	20010924	<--
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EP 1463495	A2	EP 2002-717708	20020321	<--

		WO 2002-US8938	20020321	<--
AU 2002248693	A2	AU 2002-248693	20020321	<--
MX 2003008582	A1	WO 2002-US8938	20020321	<--
		MX 2003-8582	20030922	<--
JP 2005500259	W	JP 2002-574911	20020321	<--
		WO 2002-US8938	20020321	<--
US 7012098	B2 Provisional	US 2001-278512P	20010323	<--
		US 2001-961969	20010924	<--

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002248693	A1 Based on	WO 2002076395
EP 1463495	A2 Based on	WO 2002076395
AU 2002248693	A2 Based on	WO 2002076395
MX 2003008582	A1 Based on	WO 2002076395
JP 2005500259	W Based on	WO 2002076395

PRIORITY APPLN. INFO: **US 2001-961969 20010924; US 2001-278512P 20010323**

INT. PATENT CLASSIF.:

MAIN: A61K000-00; A61K000-00000; A61K031-16; A61K031-185; A61K031-195; A61K031-198; A61K031-66

SECONDARY: A61K031-352; A61K031-382; A61K031-41; A61K031-415; A61K031-4375; A61K031-47; A61K031-55; A61K045-00; A61P035-00; A61P043-00; C07C257-14; C07C259-14; C07C317-50; C07C323-58

BASIC ABSTRACT:

WO 200276395 A UPAB: 20031006

NOVELTY - Composition (C) comprising an inducible **nitric oxide** synthase selective inhibitor (A) and a cyclooxygenase-2 inhibitor (B) or their salts or a prodrug, is new.

DETAILED DESCRIPTION - Composition (C) comprising an inducible **nitric oxide** synthase (iNOS) selective inhibitor (A) of formula (I)-(X), and a cyclooxygenase-2 (COX-2) inhibitor (B) or their salts or prodrugs, is new.

R1, R2 = H, halo or alkyl (optionally substituted by at least one halo);

R7 = H or OH;

J = OH, alkoxy or NR3R4;

R3 = H, lower alkyl, lower alkenyl or lower alkynyl;

R4 = H, heterocyclic ring (containing 1-4 O, N or S, and optionally substituted by heteroarylamino, N-aryl-N-alkylamino, N-heteroarylamino-N-alkylamino, haloalkylthio, alkanoyloxy, alkoxy, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, OH, amino, SH, NO2, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, (hetero)arylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, (hetero)arylsulfinyl, (hetero)arylsulfonyl, (halo)alkanoyl, alkenoyl, (hetero)aroyl, (hetero)aralkanoyl, (halo)alkyl, alkenyl, alkynyl, (halo)alkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydroxyheteroaralkyl, haloalkoxyalkyl, (hetero)aryl, aralkyl, (hetero)aryloxy, aralkoxy, (hetero)aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, (hetero)arylalkyl, (hetero)arylalkenyl, cyanoalkyl, dicyanoalkyl, carboxamidoalkyl, dicarboxamidoalkyl, cyanocarboalkoxyalkyl,

carboalkoxyalkyl, dicarboalkoxyalkyl, cyanocycloalkyl, dicyanocycloalkyl, carboxamidocycloalkyl, dicarboxamidocycloalkyl, carboalkoxycyanocycloalkyl, carboalkoxycycloalkyl, dicarboalkoxycycloalkyl, formylalkyl, acylalkyl, dialkoxyphosphonoalkyl, diaralkylphosphonoalkyl, phosphonoalkyl, dialkoxyphosphonoalkoxy, diaralkoxyphsphonoalkylamido, diaralkoxyphosphonoalkylamino, phosphonoalkylamino, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, guanidino, amidino or acylamino);

X = -S-, -S(O)- or -S(O)2-;

R12 = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-5C alkoxy-methyl or 1-5C alkylthio-methyl (all optionally substituted by at least one OH, alkoxy or halo);

R18 = OR24 or NR25R26;

R13 = H, OH, C(O), C(O)R27, C(O)OR28 C(R31)(R32) or C(O)SR29; or

R18+R13 = a ring;

R14 = C(O)OR33 or H;

R11, R15-R17 = H, halo, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-5C alkoxy-methyl;

R19, R20 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or 1-5C alkoxy-methyl;

R21 = H,OH, C(O)OR34, C(O)SR35 or -O-;

R22 = H,OH, C(O)OR36, C(O)SR37 or -C(O)-; or

R21+R22 = a ring;

R23 = Me;

R24 = H or 1-6C alkyl;

R25 = H, alkyl or alkoxy;

R26 = H, OH, alkyl, alkoxy, C(O)R38, C(O)OR39, C(O)SR40, cycloalkyl, heterocyclyl or (hetero)aryl;

R27-R40 = H or alkyl (optionally substituted by cycloalkyl, heterocyclyl or (hetero)aryl);

R41, R42 = H or Me;

R43, R44, R47, R48 = H, halo or 1-5C alkyl (optionally substituted by alkoxy or at least one halo);

R45, R49 = 1-5C alkyl (optionally substituted by alkoxy or at least one halo);

R46, R50, R52, R55 = 1-5C alkyl (optionally substituted by halo or alkoxy (itself optionally substituted by at least one halo);

R51, R53, R56 = H, halo or 1-5C alkyl (optionally substituted by halo or alkoxy (itself optionally substituted by at least one halo); and

R54 = halo or 1-5C alkyl (optionally substituted by halo or alkoxy (itself optionally substituted by at least one halo);

provided that:

(1) at least one of R1 or R2 = halo;

(2) when R18 = N(R30), then R13 = -C(O)-;

(3) when R18 = -O-, then R13 = -C(O)- or -C(R31)(R32);

(4) when R13 = -C(R31)(R32)- then R14 = C(O)OR33, otherwise R14 = H;

(5) when R21 = -O- then R22 = -C(O)-;

(6) when R21 = -C(O)- then R22 = -O-;

(7) R24 = 1-6C alkyl, then R24 is optionally substituted by at least one cycloalkyl, heterocyclyl or (hetero)aryl;

(8) when R25 and R26 = alkyl or alkoxy, then R25 and R26 are optionally substituted by at least one cycloalkyl, heterocyclyl or (hetero)aryl;

(9) when R25 = H then R26 = cycloalkyl, heterocyclyl or (hetero)aryl; and

(10) when R11-R40 = alkyl, alkenyl, alkynyl, alkoxy, alkylthio, cycloalkyl, heterocyclyl or (hetero)aryl, then the moiety is optionally substituted by OH, alkoxy or halo.

An INDEPENDENT CLAIM is also included for a method for the treatment or prevention of cancer comprising administration of (I)-(X).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Induced Nitric Oxide Synthase (iNOS) Inhibitor; Cyclooxygenase-2 (COX-2) Inhibitor.

Nitric oxide synthase (NOS) activity was determined by monitoring the conversion of L-(2,3-3H)-arginine to L-(2,3-3H)-citrulline using the method described in Bredt and Snyder, Proc. Natl. Acad. Sci. USA; 87, 682-685, 1990. S-(2-((1-iminoethyl)amino)ethyl)-2-methyl-L-cysteine (Ia) inhibited NOS with an IC50 of 3.1 micro M.

USE - The composition is used for treating or preventing cancer (e.g. gastrointestinal cancer, liver cancer, bladder cancer, pancreas cancer, ovary cancer, prostate cancer, cervical cancer, lung cancer, breast cancer, multiple myeloma, chronic lymphocytic leukemia, skin cancer, brain cancer, bone cancer, a leukemia, a lymphoma, epithelial cell-derived neoplasia, adenocarcinoma, renal cell carcinoma, eye cancer, Hodgkin's disease, Karposi's sarcoma, Hodgkin's lymphoma, Waldenstrom's macroglobulinemia, parathyroid cancer, penile cancer, rectal cancer, sezary syndrome, small intestine cancer, stomach cancer, vaginal cancer, vulvar cancer or Wilm's tumor), fibrosis that occurs with radiation therapy or adenomatous polyps (all claimed) including those with familial adenomatous polyposis (FAP).

ADVANTAGE - The composition improves the treatment efficacy while minimizing the toxicity and adverse side effects of each agent, and allows reduced dosages of individual chemopreventive agents whilst maintaining or improving their efficacy. The composition has improved potency and reduced dosing requirements for each active compound as compared to the therapeutic agents using the active compounds individually.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-H; B07-H; B10-A08; B10-C03; B10-C04A; B10-C04B; B10-C04C; B14-H01; B14-L06

TECH UPTX: 20031006

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: (A) May be administered in combination with a non-steroidal anti-inflammatory drug (D) or (E).

Preferred Components: (D) Is aspirin, indomethacin, sulindac, etodolac, mefenamic acid, tolmetin, ketorolac, diclofenac, ibuprofen, naproxen, fenoprofen, ketoprofen, oxaprozin, flubiprofen, piroxicam, tenoxicam, phenylbutazone, apazone, nimesulide or their salts or prodrugs.
(E) Is a compound selected from the class of chromene COX-2 selective inhibitor, a compound of formula (XI) or (XII) or their salts, meloxicam, ABT-963 or COX-189 (preferably celecoxib, valdecoxib, roficoxib, deracoxib, etericoxib, meloxicam, COX-189 or ABT-963).
A = partially unsaturated 5-6 membered heterocyclo or carbocyclic ring (optionally substituted by at least one alkyl, halo, oxo or alkoxy);
Ra = cyclohexyl, pyridinyl or phenyl (all optionally substituted by at least one (halo)alkyl, CN, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, phenylamino, NO2, alkoxyalkyl, alkylsulfinyl, halo, alkoxy or alkylthio);
Rb = alkyl or amino;
Rc = halo, alkyl, alkenyl, alkynyl, (hetero)aryl, oxo, CN, carboxyl, cyanoalkyl, heterocyclyloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, phenyl, haloalkyl, heterocyclo, cycloalkenyl, phenylalkyl, heterocyclylalkyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, phenylcarbonyl, phenylalkylcarbonyl, phenylalkenyl, alkoxyalkyl, phenylthioalkyl, phenylyloxyalkyl, alkoxyphenylalkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-phenylaminocarbonyl, N-alkyl-N-phenylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-arylalkylamino, N-alkyl-N-arylalkylamino, N-alkyl-N-arylamino,

aminoalkyl, alkylaminoalkyl, N-phenylaminoalkyl, N-phenylalkylaminoalkyl, N-alkyl-N-phenylalkylaminoalkyl, N-alkyl-N-phenylaminoalkyl, phenyloxy, phenylalkoxy, phenylthio, phenylalkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-phenylaminosulfonyl, phenylsulfonyl or N-alkyl-N-phenylaminosulfonyl;
Rd = H or halo;
G = O, S or N-alkyl;
Re = H or aryl;
Rf = carboxyl, aminocarbonyl, alkylsulfonylaminocarbonyl or alkoxycarbonyl;
Rg = (halo)alkyl, aralkyl, cycloalkyl or aryl (optionally substituted by at least one alkylthio, NO2 or alkylsulfonyl); and
Rh = H, halo, (halo)alkyl, aralkyl, (halo)alkoxy, (hetero)aryloxy, (hetero)aralkyloxy, alkylamino, (hetero)arylamino, aralkylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, (hetero)arylaminosulfonyl, (hetero)aralkylaminosulfonyl, heterocyclosulfonyl, alkylsulfonyl, hydroxyarylcarbonyl, nitroaryl, optionally substituted (hetero)aryl, aralkylcarbonyl, (hetero)arylcarbonyl, aminocarbonyl or alkylcarbonyl; or
Rh+ ring E = naphthyl or its isomer.

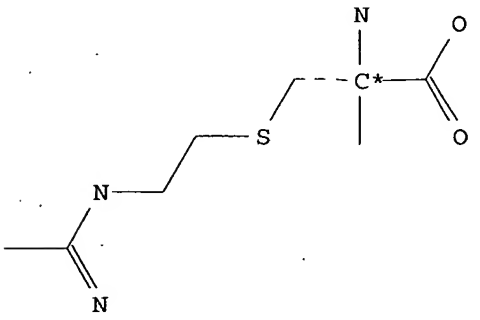
ABEX UPTX: 20031006

ADMINISTRATION - Administration of (A) is 0.001-2500 mg/kg/day. Administration of (B) is 0.3-100 (preferably 3-10) mg/kg/day. The Composition is administered orally, intravenously, subcutaneously, rectally, topically, buccally (e.g. sublingually), intramuscularly or intradermally.

DCSE 465473-3-0-0

CN.S 3-(2-Acetimidoylamino-ethylsulfanyl)-2-amino-2-methyl-propionic acid

SDCN RA5R8T



```
=> d que l32
L16             QUE  ABB=ON  PLU=ON  PHARMACIA/CS,SO,PA
L18             QUE  ABB=ON  PLU=ON  ?CRYST?
L19             QUE  ABB=ON  PLU=ON  MELT? OR MP OR (M(W)P)
L20             QUE  ABB=ON  PLU=ON  (WATER OR H2O OR MOISTURE)(4A)(?SORB
                ? OR ?SORP? OR ABSORB? OR ABSORP?)
L21             QUE  ABB=ON  PLU=ON  ?SOLUBIL? OR ?SOLUBL?
L22             QUE  ABB=ON  PLU=ON  XRAY OR (X(W)RAY) OR DIFFRAC? OR (PO
                WDER(2A)PATTERN)
L23             QUE  ABB=ON  PLU=ON  RAMAN
L24             QUE  ABB=ON  PLU=ON  ?ANALY?
L25             QUE  ABB=ON  PLU=ON  TGA OR THERMAL? OR THERMO? OR DSC OR
                 CALORIM?
L26          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BROSTROM, L?/AU
L27             QUE  ABB=ON  PLU=ON  ?MALEAT? OR ?MALEIC?
L28           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L27
L29          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND (L18 OR L19 OR L20 OR
                L21 OR L22 OR L23 OR L24 OR L25)
L30           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND (L18 OR L22)
L31           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND L16
L32           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 OR L31


=> d que l45
L2            1 SEA FILE=WPIX ABB=ON  PLU=ON  US2004-797348/APPS
L41           8 SEA FILE=WPIX ABB=ON  PLU=ON  BROSTROM, L?/AU
L42           8 SEA FILE=WPIX ABB=ON  PLU=ON  L41 AND ((?MALEAT?/BIX OR
                ?MALEIC?/BIX) OR (?CRYST?/BIX) OR (XRAY/BIX OR (X/BIX(W)RAY/BIX
                ) OR DIFFRAC?/BIX OR (POWDER/BIX(2A)PATTERN/BIX)))
L44           4 SEA FILE=WPIX ABB=ON  PLU=ON  L42 AND ((?MALEAT?/BIX OR
                ?MALEIC?/BIX) OR ((NITRIC/BIX(W)OXIDE/BIX) OR (NO/BIX(5A)SYNTHA
                S?/BIX)))
L45           4 SEA FILE=WPIX ABB=ON  PLU=ON  L44 OR L2


=> d his l65

     (FILE 'MEDLINE, BIOSIS, PASCAL, JICST-EPLUS, EMBASE, LIFESCI, DRUGU,
     DRUGB, VETU, VETB, SCISEARCH, CONF, CONFSCI, DISSABS' ENTERED AT 09:33:00
     ON 24 MAY 2006)
L65           3 S L62-L64

=> d que l65
L15             QUE  ABB=ON  PLU=ON  BROSTROM, L?/AU
L18             QUE  ABB=ON  PLU=ON  ?CRYST?
L22             QUE  ABB=ON  PLU=ON  XRAY OR (X(W)RAY) OR DIFFRAC? OR (PO
                WDER(2A)PATTERN)
L27             QUE  ABB=ON  PLU=ON  ?MALEAT? OR ?MALEIC?
L43             QUE  ABB=ON  PLU=ON  (NITRIC(W)OXIDE) OR (NO(5A)SYNTHAS?)
L61         447 SEA L15
L62           0 SEA L61 AND (L27 OR ?BUTEN?)
L63           1 SEA L61 AND L43
L64           3 SEA L61 AND (L18 OR L22)
L65           3 SEA (L62 OR L63 OR L64)

=> dup rem l32 l45 l65
DUPLICATE IS NOT AVAILABLE IN 'CONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
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FILE 'HCAPLUS' ENTERED AT 09:45:54 ON 24 MAY 2006
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FILE 'SCISEARCH' ENTERED AT 09:45:54 ON 24 MAY 2006
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PROCESSING COMPLETED FOR L45
PROCESSING COMPLETED FOR L65
L67             7 DUP REM L32 L45 L65 (4 DUPLICATES REMOVED)
                  ANSWERS '1-4' FROM FILE HCAPLUS
                  ANSWERS '5-6' FROM FILE MEDLINE
                  ANSWER '7' FROM FILE SCISEARCH

=> file stnguide
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 19, 2006 (20060519/UP).

=> d ibib ed ab 1-7
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, SCISEARCH' - CONTINUE? (Y)/N:y


L67  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:780659  HCAPLUS
DOCUMENT NUMBER:          141:261066
TITLE:                    S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine
                          maleate hydrochloride crystalline
                          salt
INVENTOR(S):              Sheikh, Ahmad; Brostrom, Lyle R.; Czyzewski,
                          Ann M.; Zia, Vahid
PATENT ASSIGNEE(S):       Pharmacia Corporation, USA
SOURCE:                   PCT Int. Appl., 84 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004080956         A1    20040923    WO 2004-IB678            20040304
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
```

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004220266	A1	20040923	AU 2004-220266	20040304
CA 2518745	AA	20040923	CA 2004-2518745	20040304
EP 1603872	A1	20051214	EP 2004-717188	20040304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008226	A	20060301	BR 2004-8226	20040304
US 2005038120	A1	20050217	US 2004-797462	20040310
NL 1025691	A1	20040914	NL 2004-1025691	20040311
NO 2005004645	A	20051125	NO 2005-4645	20051010
PRIORITY APPLN. INFO.:			US 2003-453496P P	20030311
			WO 2004-IB678 A	20040304

ED Entered STN: 24 Sep 2004

AB The invention relates to **crystalline** S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine **maleate** hydrochloride (I) for use in treating conditions characterized by an overexpression of nitric oxide from the inducible isoform of nitric oxide synthase. The examples describe methods used to make **crystalline** I that may be arranged as generally orderly packed agglomerates, which are particularly useful in making pharmaceutical compns.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:780658 HCAPLUS

DOCUMENT NUMBER: 141:261065

TITLE: S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine **maleate** form II **crystalline** salt

INVENTOR(S): **Brostrom, Lyle R.**

PATENT ASSIGNEE(S): **Pharmacia** Corporation, USA

SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080955	A1	20040923	WO 2004-IB627	20040304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2518737	AA	20040923	CA 2004-2518737	20040304
EP 1603871	A1	20051214	EP 2004-717172	20040304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008483	A	20060404	BR 2004-8483	20040304
US 2004204488	A1	20041014	US 2004-797348	20040310

PRIORITY APPLN. INFO.: US 2003-453796P P 20030311
WO 2004-IB627 W 20040304

ED Entered STN: 24 Sep 2004
AB The invention relates to a method of preparing **crystalline** S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine (I) **maleate** for use in decreasing nitric oxide production in a subject. Thus, I **maleate melting** at 123 °C was obtained by **crystallization** from an acetonitrile solution Free base I was obtained by reaction of N-Boc-cysteamine (Boc = tert-butoxycarbonyl) with chloroacetone then sodium cyanide and ammonium carbonate, chromatog. separation of enantiomeric imidazolidinedione derivs., and reaction with Et acetimidate hydrochloride. **Crystalline** I **maleate** was **analyzed** by **X-ray** powder **diffraction** and **thermal anal.**
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:780657 HCAPLUS
DOCUMENT NUMBER: 141:261064
TITLE: S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine **maleate** form II **crystalline** salt
INVENTOR(S): Sheikh, Ahmad; **Brostrom, Lyle**
PATENT ASSIGNEE(S): **Pharmacia** Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080954	A1	20040923	WO 2004-IB697	20040304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2517728	AA	20040923	CA 2004-2517728	20040304
EP 1603869	A1	20051214	EP 2004-717175	20040304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008177	A	20060301	BR 2004-8177	20040304
US 2004209956	A1	20041021	US 2004-797500	20040310

PRIORITY APPLN. INFO.: US 2003-453782P P 20030311
WO 2004-IB697 W 20040304

ED Entered STN: 24 Sep 2004
AB The invention relates to a method of preparing **crystalline** S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine (I) **maleate** for use in decreasing nitric oxide production in a subject. Thus, I **maleate melting** at 77.69 °C was obtained by **crystallization** from an acetonitrile solution Free base I was obtained by reaction of N-Boc-cysteamine (Boc = tert-butoxycarbonyl) with

chloroacetone then sodium cyanide and ammonium carbonate, chromatog. separation of enantiomeric imidazolidinedione derivs., and reaction with Et acetimidate hydrochloride. **Crystalline** I **maleate** was **analyzed** by **X-ray** powder **diffraction** and **thermal anal.**

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:780656 HCAPLUS
DOCUMENT NUMBER: 141:261063
TITLE: S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine salicylate monohydrate **crystalline** salt
INVENTOR(S): **Brostrom, Lyle R.**
PATENT ASSIGNEE(S): **Pharmacia** Corporation, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080953	A1	20040923	WO 2004-IB645	20040304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2517723	AA	20040923	CA 2004-2517723	20040304
EP 1603870	A1	20051214	EP 2004-717181	20040304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008182	A	20060321	BR 2004-8182	20040304
US 2005239754	A1	20051027	US 2004-797349	20040310
PRIORITY APPLN. INFO.:			US 2003-453772P P	20030311
			WO 2004-IB645 W	20040304

ED Entered STN: 24 Sep 2004
AB The invention relates to a method of preparing **crystalline** S-[2-[(1-iminoethyl)amino]ethyl]-2-methyl-L-cysteine (I) salicylate monohydrate for use in decreasing nitric oxide production in a subject. Thus, **crystallization** of I salicylate monohydrate occurred from a solution containing I zwitterion and salicylic acid in DMF with addition of THF. Free base I was obtained by reaction of N-Boc-cysteamine (Boc = tert-butoxycarbonyl) with chloroacetone then sodium cyanide and ammonium carbonate, chromatog. separation of enantiomeric imidazolidinedione derivs., and reaction with Et acetimidate hydrochloride. **Crystalline** I salicylate monohydrate was **analyzed** by **X-ray** powder **diffraction** and **thermal anal.**

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 5 OF 7 MEDLINE on STN
ACCESSION NUMBER: 90079630 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2293629
TITLE: Electromyogram (EMG) recordings from the subscapularis muscle: description of a technique.
AUTHOR: Nemeth G; Kronberg M; **Brostrom L A**
CORPORATE SOURCE: Department of Orthopaedics, Karolinska Hospital, Stockholm, Sweden.
SOURCE: Journal of orthopaedic research : official publication of the Orthopaedic Research Society, (1990 Jan) Vol. 8, No. 1, pp. 151-3.
Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199001
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 24 Jan 1990
ED Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 24 Jan 1990
AB Operative treatments for recurrent dislocation of the shoulder usually focus on the subscapularis muscle because it is supposed to contribute to the joint stability. It is of clinical interest to record the EMG from the subscapularis muscle in order to interpret its function. The purpose of the present study was to describe a safe and reliable route to reach the muscle, deeply located between the scapula and the thoracic cage, with fine-wire EMG electrodes. Twenty-four shoulders were investigated in 12 volunteers. A hypodermic needle containing bipolar fine-wire electrodes was inserted in the posterior axillary line with the subjects in the supine position, and the arm held in an abducted and externally rotated position. Three criteria confirmed the location of the electrodes: experience of periosteal pain when the needle reached the costal surface of the scapula, drawing-in of the wires 3-4 cm when the subject adducted his arm, thereby rotating his scapula downward, and raw EMG recorded during typical movements. Additionally, in four shoulders, the electrode location was checked with computed tomography. There were no complications from this technique, and the subjects felt no pain from the fine-wire electrodes during arm movements. We conclude that the described technique is a safe and reliable method of reaching the subscapularis muscle with EMG electrodes.

L67 ANSWER 6 OF 7 MEDLINE on STN
ACCESSION NUMBER: 90122400 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2611057
TITLE: Radiologic assessment of humeral head retroversion. Description of a new method.
AUTHOR: Soderlund V; Kronberg M; **Brostrom L A**
CORPORATE SOURCE: Department of Diagnostic Radiology, Karolinska Sjukhuset, Stockholm, Sweden.
SOURCE: Acta radiologica (Stockholm, Sweden : 1987), (1989 Sep-Oct) Vol. 30, No. 5, pp. 501-5.
Journal code: 8706123. ISSN: 0284-1851.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003

ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 1 Mar 1990

ED Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 1 Mar 1990

AB A radiologic method for assessment of the humeral head retroversion angle has been developed using one radiograph obtained in the semi-axial view. Validity and reliability of the method has been tested. In five healthy volunteers both shoulders were examined both with CT and with the new radiographic method. The average difference in angle determinations between the methods was 1.5 degrees and the maximum difference was 2 degrees. Angle determination on radiographs from 22 healthy shoulders was performed by two independent radiologists. The coefficient of variation for intraobserver measurements was 2.8 per cent and for interobserver measurements it was 4.6 per cent. Three isolated humerus bones were examined in multiple semi-axial projections and the humeral head retroversion was measured. The effect of humeral position (flexion, extension, abduction) on angle assessments was analyzed. A method error exceeding 2 degrees was only seen when the specimens were in an extended or extremely abducted position. It is concluded that with the arm in the correct position measurements of humeral head retroversion can be performed with this method with high accuracy.

L67 ANSWER 7 OF 7 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:220929 SCISEARCH
THE GENUINE ARTICLE: HL099
TITLE: THE **X-RAY** EXCITED AUGER-ELECTRON SPECTRUM OF NO AND POTENTIAL CURVES AND PHOTODISSOCIATION OF THE NO2+ ION
AUTHOR: PETTERSSON L G M (Reprint); KARLSSON L; KEANE M P; DEBRITO A N; CORREIA N; LARSSON M; **BROSTROM L**; MANNERVIK S; SVENSSON S
CORPORATE SOURCE: UNIV STOCKHOLM, DEPT THEORET PHYS, VANADISVAGEN 9, S-11346 STOCKHOLM, SWEDEN (Reprint); UNIV UPPSALA, DEPT PHYS, S-75121 UPPSALA, SWEDEN; ROYAL INST TECHNOL, DEPT PHYS 1, S-10044 STOCKHOLM 70, SWEDEN; MANNE SIEGBAHN INST PHYS, S-10405 STOCKHOLM, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: JOURNAL OF CHEMICAL PHYSICS, (1 APR 1992) Vol. 96, No. 7, pp. 4884-4895.
ISSN: 0021-9606.
PUBLISHER: AMER INST PHYSICS, CIRCULATION FULFILLMENT DIV, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2999.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 65
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

ED Entered STN: 1994
Last Updated on STN: 1994

AB A study of the NO2+ ion by means of Auger spectroscopy, fast ion beam laser spectroscopy and ab initio calculations is reported. The photon induced Auger spectrum of NO was recorded. Potential curves for a number of electronic states of NO2+ were calculated by the complete active space SCF method in order to facilitate an analysis of the Auger spectrum. A photoabsorption spectrum of NO2+ was observed by means of photofragment

kinetic energy spectroscopy and assigned to the A (2)PI <-- X (2)SIGMA+ transition. The two different experimental methods both give a value of 38.6 eV for the appearance energy of NO2+, which is entirely consistent with recent photoionization and double charge transfer results.

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=> d his ful

     (FILE 'HOME' ENTERED AT 08:22:39 ON 24 MAY 2006)

     FILE 'ZCAPLUS' ENTERED AT 08:22:47 ON 24 MAY 2006
               E US2004-797348/APPS

     FILE 'HCAPLUS' ENTERED AT 08:23:05 ON 24 MAY 2006
L1             1 SEA ABB=ON  PLU=ON  US2004-797348/APPS
               SAVE TEMP L1 VAL348HCAAPP/A

     FILE 'STNGUIDE' ENTERED AT 08:23:19 ON 24 MAY 2006

     FILE 'HCAPLUS' ENTERED AT 08:23:30 ON 24 MAY 2006
               D IBIB ED AB IND

     FILE 'STNGUIDE' ENTERED AT 08:23:30 ON 24 MAY 2006

     FILE 'WPIX' ENTERED AT 08:25:00 ON 24 MAY 2006
L2             1 SEA ABB=ON  PLU=ON  US2004-797348/APPS
               SAVE TEMP L2 VAL348WPIAPP/A
               D IALL CODE

     FILE 'STNGUIDE' ENTERED AT 08:25:27 ON 24 MAY 2006

     FILE 'REGISTRY' ENTERED AT 08:26:04 ON 24 MAY 2006

     FILE 'HCAPLUS' ENTERED AT 08:26:09 ON 24 MAY 2006
L3             TRA PLU=ON  L1 1- RN :       14 TERMS

     FILE 'REGISTRY' ENTERED AT 08:26:11 ON 24 MAY 2006
L4            14 SEA ABB=ON  PLU=ON  L3
               SAVE TEMP L4 VAL348REGAPP/A
               D SCAN

     FILE 'STNGUIDE' ENTERED AT 08:26:41 ON 24 MAY 2006

     FILE 'LREGISTRY' ENTERED AT 08:27:28 ON 24 MAY 2006
L5             STR

     FILE 'REGISTRY' ENTERED AT 08:30:12 ON 24 MAY 2006
L6             9 SEA SSS SAM L5
               D SCAN
               D QUE STAT

     FILE 'STNGUIDE' ENTERED AT 08:31:27 ON 24 MAY 2006

     FILE 'REGISTRY' ENTERED AT 08:32:43 ON 24 MAY 2006
L7           163 SEA SSS FUL L5
               SAVE TEMP L7 VAL348PSET1/A

     FILE 'LREGISTRY' ENTERED AT 08:33:12 ON 24 MAY 2006
L8             STR

     FILE 'REGISTRY' ENTERED AT 08:35:30 ON 24 MAY 2006
L9            50 SEA SSS SAM L8
L10            0 SEA SUB=L7 SSS SAM L8
               D QUE STAT L9
L11            4 SEA SUB=L7 SSS FUL L8
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                D SCAN
                SAVE TEMP L11 VAL348RSET1/A

     FILE 'STNGUIDE' ENTERED AT 08:38:10 ON 24 MAY 2006
                D SAVED

     FILE 'REGISTRY' ENTERED AT 08:38:41 ON 24 MAY 2006
L12            14 SEA ABB=ON  PLU=ON  L3
L13             1 SEA ABB=ON  PLU=ON  L11 AND L12

     FILE 'STNGUIDE' ENTERED AT 08:38:55 ON 24 MAY 2006
                D QUE STAT L7
                D QUE STAT L11

     FILE 'REGISTRY' ENTERED AT 08:39:40 ON 24 MAY 2006
                D IDE L11 1-4

     FILE 'STNGUIDE' ENTERED AT 08:39:41 ON 24 MAY 2006

     FILE 'STNGUIDE' ENTERED AT 08:39:46 ON 24 MAY 2006
                D QUE L7
                D QUE L11

     FILE 'BEILSTEIN' ENTERED AT 08:41:40 ON 24 MAY 2006
L14             0 SEA SSS FUL L5
                SAVE TEMP L14 VAL348BEIP/A

     FILE 'STNGUIDE' ENTERED AT 08:42:14 ON 24 MAY 2006

     FILE 'ZCAPLUS' ENTERED AT 08:42:36 ON 24 MAY 2006
L15             QUE ABB=ON  PLU=ON  BROSTROM, L?/AU
L16             QUE ABB=ON  PLU=ON  PHARMACIA/CS,SO,PA
L17             QUE ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY<2004
                OR REVIEW/DT
L18             QUE ABB=ON  PLU=ON  ?CRYST?
L19             QUE ABB=ON  PLU=ON  MELT? OR MP OR (M(W)P)
L20             QUE ABB=ON  PLU=ON  (WATER OR H2O OR MOISTURE)(4A)(?SORB? OR
                ?SORP? OR ABSORB? OR ABSORP?)
L21             QUE ABB=ON  PLU=ON  ?SOLUBIL? OR ?SOLUBL?
L22             QUE ABB=ON  PLU=ON  XRAY OR (X(W)RAY) OR DIFFRAC? OR (POWDER(2A
                )PATTERN)
L23             QUE ABB=ON  PLU=ON  RAMAN
L24             QUE ABB=ON  PLU=ON  ?ANALY?
L25             QUE ABB=ON  PLU=ON  TGA OR THERMAL? OR THERMO? OR DSC OR
                CALORIM?

     FILE 'HCAPLUS' ENTERED AT 08:47:16 ON 24 MAY 2006
L26            16 SEA ABB=ON  PLU=ON  BROSTROM, L?/AU
L27             QUE ABB=ON  PLU=ON  ?MALEAT? OR ?MALEIC?
L28             3 SEA ABB=ON  PLU=ON  L26 AND L27
L29            12 SEA ABB=ON  PLU=ON  L26 AND (L18 OR L19 OR L20 OR L21 OR L22
                OR L23 OR L24 OR L25)
L30             8 SEA ABB=ON  PLU=ON  L29 AND (L18 OR L22)
L31             4 SEA ABB=ON  PLU=ON  L30 AND L16
L32             4 SEA ABB=ON  PLU=ON  L28 OR L31
                SAVE TEMP L32 VAL348HCAINV/A
                D SCAN

     FILE 'STNGUIDE' ENTERED AT 08:49:21 ON 24 MAY 2006
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     FILE 'HCAPLUS' ENTERED AT 08:50:12 ON 24 MAY 2006
L*** DEL      16 S L7
L33            5 SEA ABB=ON  PLU=ON  L11
L34            3 SEA ABB=ON  PLU=ON  L33 AND (L18 OR L19 OR L20 OR L21 OR L22
                 OR L23 OR L24 OR L25)
L35            5 SEA ABB=ON  PLU=ON  L33 OR L34
L36            5 SEA ABB=ON  PLU=ON  L35 AND L17
                 SAVE TEMP L36 VAL348HCA1B VAL348HCA1B/A
L37            0 SEA ABB=ON  PLU=ON  L35 NOT L36
                 D SCAN L36

     FILE 'STNGUIDE' ENTERED AT 08:52:07 ON 24 MAY 2006

     FILE 'HCAPLUS' ENTERED AT 08:52:25 ON 24 MAY 2006
L38            2 SEA ABB=ON  PLU=ON  L36 NOT L32

     FILE 'STNGUIDE' ENTERED AT 08:52:36 ON 24 MAY 2006
                 D SAVED

     FILE 'USPATFULL, USPAT2' ENTERED AT 08:53:30 ON 24 MAY 2006
L39           11 SEA ABB=ON  PLU=ON  L11
L40           11 SEA ABB=ON  PLU=ON  L39 AND (AY<2004 OR PY<2004 OR PRY<2004)
                 SAVE TEMP L40VAL348USP1B/A L40 VAL348USP1B/A

     FILE 'STNGUIDE' ENTERED AT 08:54:27 ON 24 MAY 2006

     FILE 'WPIX' ENTERED AT 08:56:22 ON 24 MAY 2006
L41            8 SEA ABB=ON  PLU=ON  BROSTROM, L?/AU
L42            8 SEA ABB=ON  PLU=ON  L41 AND ((?MALEAT?/BIX OR ?MALEIC?/BIX) OR
                 (?CRYST?/BIX) OR (XRAY/BIX OR (X/BIX(W)RAY/BIX) OR DIFFRAC?/BIX
                  OR (POWDER/BIX(2A)PATTERN/BIX)))
                 D TRI 1-8

     FILE 'ZCAPLUS' ENTERED AT 08:58:39 ON 24 MAY 2006
L43              QUE ABB=ON  PLU=ON  (NITRIC(W)OXIDE) OR (NO(5A)SYNTHAS?)

     FILE 'WPIX' ENTERED AT 08:59:24 ON 24 MAY 2006
L44            4 SEA ABB=ON  PLU=ON  L42 AND ((?MALEAT?/BIX OR ?MALEIC?/BIX) OR
                 ((NITRIC/BIX(W)OXIDE/BIX) OR (NO/BIX(5A)SYNTHAS?/BIX)))
L45            4 SEA ABB=ON  PLU=ON  L44 OR L2
                 SAVE TEMP L45 VAL348WPIINV/A
L46            4 SEA SSS SAM L5
                 D QUE STAT
L47           34 SEA SSS FUL L5
                 SAVE TEMP L47 VAL348WPIPS/A
L48           14 SEA ABB=ON  PLU=ON  L47/DCR
                 SELECT L48 1- DCN
                 SELECT L47 1- SDCN
L49           14 SEA ABB=ON  PLU=ON  (RACSJE/DCN OR RACSJG/DCN OR RACSJJ/DCN OR
                 RACSJL/DCN OR RACSJU/DCN OR RACSJW/DCN OR RACSJY/DCN OR
                 RAFIL7/DCN OR RAFI3K/DCN OR RAFI4G/DCN OR RAFI57/DCN OR
                 RAHF7P/DCN OR RAHF7Q/DCN OR RAHF7S/DCN OR RAHF7T/DCN OR
                 RAHF7V/DCN OR RA5HUE/DCN OR RA5HUF/DCN OR RA5R8T/DCN OR
                 RA5R8W/DCN OR RA5R8X/DCN OR RA5R8Y/DCN OR RA5R8Z/DCN OR
                 RA5R9A/DCN OR RA5R9C/DCN OR RA5R9G/DCN OR RA5R9H/DCN OR
                 RA5R91/DCN OR RA5R92/DCN OR RA5R93/DCN OR RA5R96/DCN OR
                 RA5R97/DCN OR RA5R98/DCN OR RA5R99/DCN)
L50           14 SEA ABB=ON  PLU=ON  L48 OR L49
L51           14 SEA ABB=ON  PLU=ON  L50 AND ((?CRYST?/BIX) OR (MELT?/BIX OR
                 MP/BIX OR (M/BIX(W)P/BIX)) OR ((WATER/BIX OR H2O/BIX OR
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                MOISTURE/BIX)(4A)(?SORB?/BIX OR ?SORP?/BIX OR ABSORB?/BIX OR
                ABSORP?/BIX)) OR (?SOLUBIL?/BIX OR ?SOLUBL?/BIX) OR (XRAY/BIX
                OR (X/BIX(W)RAY/BIX) OR DIFFRAC?/BIX OR (POWDER/BIX(2A)PATTERN/
                BIX)) OR (RAMAN/BIX) OR (?ANALY?/BIX) OR (TGA/BIX OR THERMAL?/B
                IX OR THERMO?/BIX OR DSC/BIX OR CALORIM?/BIX) OR ((NITRIC/BIX(W
                )OXIDE/BIX) OR (NO/BIX(5A)SYNTHAS?/BIX)))
L52          14 SEA ABB=ON  PLU=ON  L50 OR L51
L53          14 SEA ABB=ON  PLU=ON  L52 AND (AY<2004 OR PY<2004 OR PRY<2004)
                SAVE TEMP L53 VAL348WPI1B VAL348WPI1B/A
L54           0 SEA ABB=ON  PLU=ON  L53 NOT L52
L55           0 SEA ABB=ON  PLU=ON  L52 NOT L53
L56          10 SEA ABB=ON  PLU=ON  L53 NOT L45
                D TRI 1-10
L57           6 SEA ABB=ON  PLU=ON  L53 AND (?MALEAT?/BIX OR ?MALEIC?/BIX)
L58           0 SEA ABB=ON  PLU=ON  L53 AND ?BUTENOATE?
L59           0 SEA ABB=ON  PLU=ON  L53 AND ?BUTENOATE?/BIX
L60          14 SEA ABB=ON  PLU=ON  L53 OR (L57 OR L58 OR L59)
                SAVE TEMP L60 VAL348WPI1B/A

     FILE 'STNGUIDE' ENTERED AT 09:31:37 ON 24 MAY 2006
                D SAVED

     FILE 'MEDLINE, BIOSIS, PASCAL, JICST-EPLUS, EMBASE, LIFESCI, DRUGU,
     DRUGB, VETU, VETB, SCISEARCH, CONF, CONFSCI, DISSABS' ENTERED AT 09:33:00
     ON 24 MAY 2006
L61         447 SEA ABB=ON  PLU=ON  L15
L62           0 SEA ABB=ON  PLU=ON  L61 AND (L27 OR ?BUTEN?)
L63           1 SEA ABB=ON  PLU=ON  L61 AND L43
L64           3 SEA ABB=ON  PLU=ON  L61 AND (L18 OR L22)
L65           3 SEA ABB=ON  PLU=ON  (L62 OR L63 OR L64)
                D SCAN
                SAVE TEMP L65 VAL348MULINV/A

     FILE 'STNGUIDE' ENTERED AT 09:37:30 ON 24 MAY 2006
                D SAVED
                D QUE STAT L14
                D QUE STAT L36
                D QUE NOS L40
                D QUE STAT L47
                D QUE NOS L60

     FILE 'HCAPLUS, USPATFULL, USPAT2, WPIX' ENTERED AT 09:40:40 ON 24 MAY 2006
L66          20 DUP REM L36 L40 L60 (10 DUPLICATES REMOVED)
                     ANSWERS '1-5' FROM FILE HCAPLUS
                     ANSWERS '6-13' FROM FILE USPATFULL
                     ANSWERS '14-20' FROM FILE WPIX

     FILE 'STNGUIDE' ENTERED AT 09:40:46 ON 24 MAY 2006

     FILE 'HCAPLUS, USPATFULL, WPIX' ENTERED AT 09:41:17 ON 24 MAY 2006
                D IBIB ED AB HITIND HITSTR

     FILE 'STNGUIDE' ENTERED AT 09:41:19 ON 24 MAY 2006

     FILE 'HCAPLUS, USPATFULL, WPIX' ENTERED AT 09:41:46 ON 24 MAY 2006
                D IBIB ED AB HITIND HITSTR 2-5

     FILE 'STNGUIDE' ENTERED AT 09:41:49 ON 24 MAY 2006

     FILE 'HCAPLUS, USPATFULL, WPIX' ENTERED AT 09:42:38 ON 24 MAY 2006
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D IBIB AB HITSTR 6-13

FILE 'STNGUIDE' ENTERED AT 09:42:41 ON 24 MAY 2006

FILE 'HCAPLUS, USPATFULL, WPIX' ENTERED AT 09:43:29 ON 24 MAY 2006
D IALL ABEQ TECH ABEX HITSTR 14

FILE 'STNGUIDE' ENTERED AT 09:43:31 ON 24 MAY 2006

FILE 'HCAPLUS, USPATFULL, WPIX' ENTERED AT 09:43:55 ON 24 MAY 2006
D IALL ABEQ TECH ABEX HITSTR 15-20

FILE 'STNGUIDE' ENTERED AT 09:44:03 ON 24 MAY 2006
D QUE L32
D QUE L45
D QUE L65

FILE 'HCAPLUS, WPIX, MEDLINE, SCISEARCH' ENTERED AT 09:45:54 ON 24 MAY 2006
L67 7 DUP REM L32 L45 L65 (4 DUPLICATES REMOVED)
ANSWERS '1-4' FROM FILE HCAPLUS
ANSWERS '5-6' FROM FILE MEDLINE
ANSWER '7' FROM FILE SCISEARCH

FILE 'STNGUIDE' ENTERED AT 09:46:00 ON 24 MAY 2006

FILE 'HCAPLUS, MEDLINE, SCISEARCH' ENTERED AT 09:46:09 ON 24 MAY 2006
D IBIB ED AB 1-7

FILE 'STNGUIDE' ENTERED AT 09:46:10 ON 24 MAY 2006

FILE HOME

FILE ZCAPLUS

FILE COVERS 1907 - 24 May 2006 VOL 144 ISS 22
FILE LAST UPDATED: 23 May 2006 (20060523/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE HCAPLUS

FILE COVERS 1907 - 24 May 2006 VOL 144 ISS 22
FILE LAST UPDATED: 23 May 2006 (20060523/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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substance identification.

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 19, 2006 (20060519/UP).

FILE WPIX
FILE LAST UPDATED: 18 MAY 2006 <20060518/UP>
MOST RECENT DERWENT UPDATE: 200632 <200632/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 23 MAY 2006 HIGHEST RN 885357-09-5
DICTIONARY FILE UPDATES: 23 MAY 2006 HIGHEST RN 885357-09-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005. A new display format, IDERL, is now      *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE LREGISTRY
LREGISTRY IS A STATIC LEARNING FILE

NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

FILE BEILSTEIN
FILE LAST UPDATED ON MARCH 15, 2006

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,516,393 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

****
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *
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NEW
*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**
*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 May 2006 (20060518/PD)
FILE LAST UPDATED: 18 May 2006 (20060518/ED)
HIGHEST GRANTED PATENT NUMBER: US7047565
HIGHEST APPLICATION PUBLICATION NUMBER: US2006107430
CA INDEXING IS CURRENT THROUGH 18 May 2006 (20060518/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 May 2006 (20060518/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 23 May 2006 (20060523/PD)

FILE LAST UPDATED: 23 May 2006 (20060523/ED)
HIGHEST GRANTED PATENT NUMBER: US2006027591
HIGHEST APPLICATION PUBLICATION NUMBER: US2006106932
CA INDEXING IS CURRENT THROUGH 23 May 2006 (20060523/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 23 May 2006 (20060523/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE MEDLINE
FILE LAST UPDATED: 23 MAY 2006 (20060523/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 17 May 2006 (20060517/ED)

FILE PASCAL
FILE LAST UPDATED: 22 MAY 2006 <20060522/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE IN THE BASIC INDEX (/BI) FIELD <<<

FILE JICST-EPLUS
FILE COVERS 1985 TO 15 MAY 2006 (20060515/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE EMBASE
FILE COVERS 1974 TO 23 May 2006 (20060523/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE LIFESCI
FILE COVERS 1978 TO 12 May 2006 (20060512/ED)

FILE DRUGU
FILE LAST UPDATED: 19 MAY 2006 <20060519/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE DRUGB
>>> FILE COVERS 1964 TO 1982 - CLOSED FILE <<<

FILE VETU
FILE LAST UPDATED: 02 JAN 2002 <20020102/UP>
FILE COVERS 1983-2001

FILE VETB
FILE LAST UPDATED: 25 SEP 94 <940925/UP>
FILE COVERS 1968-1982

FILE SCISEARCH

FILE COVERS 1974 TO 18 May 2006 (20060518/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE CONF
FILE LAST UPDATED: 23 DEC 2005 <20051223/UP>
FILE COVERS 1976 TO 2005.

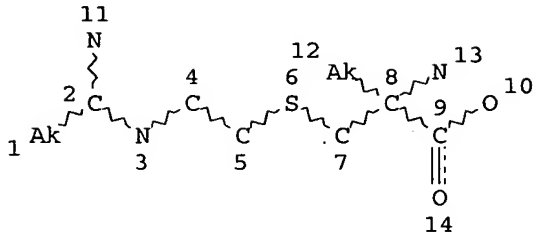
<<< CONF IS NO LONGER BEING UPDATED AS OF JANUARY 2006 >>>

FILE CONFSCI
FILE COVERS 1973 TO 10 Apr 2006 (20060410/ED)

CSA has resumed updates, see NEWS FILE

FILE DISSABS
FILE COVERS 1861 TO 28 APR 2006 (20060428/ED)

=> => d que stat l69
L5 STR



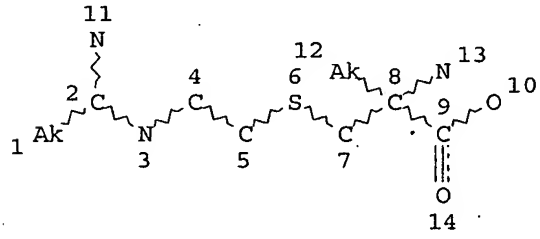
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 1
CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 11
CONNECT IS E1 RC AT 12
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L69 14 SEA FILE=MARPAT SSS FUL L5

100.0% PROCESSED 44963 ITERATIONS (9 INCOMPLETE) 14 ANSWERS
SEARCH TIME: 00.00.13

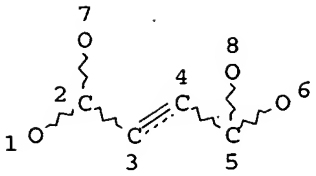
=> d que stat l71
L5 STR



NODE ATTRIBUTES:
CONNECT IS E1 RC AT 1
CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 11
CONNECT IS E1 RC AT 12
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L8 STR



```
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   1
CONNECT IS E1  RC AT   6
CONNECT IS E1  RC AT   7
CONNECT IS E1  RC AT   8
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L69          14 SEA FILE=MARPAT SSS FUL L5
L71           0 SEA FILE=MARPAT SUB=L69 SSS FUL L8

100.0% PROCESSED      12 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01


=> d his ful l68-

     (FILE 'HCAPLUS, WPIX, MEDLINE, SCISEARCH' ENTERED AT 09:45:54 ON 24 MAY
     2006)
                    ANSWERS '1-4' FROM FILE HCAPLUS
                    ANSWERS '5-6' FROM FILE MEDLINE
                    ANSWER '7' FROM FILE SCISEARCH

     FILE 'STNGUIDE' ENTERED AT 09:46:00 ON 24 MAY 2006

     FILE 'HCAPLUS, MEDLINE, SCISEARCH' ENTERED AT 09:46:09 ON 24 MAY 2006
               D IBIB ED AB 1-7

     FILE 'STNGUIDE' ENTERED AT 09:46:10 ON 24 MAY 2006

     FILE 'MARPAT' ENTERED AT 09:47:17 ON 24 MAY 2006
L68             0 SEA SSS SAM L5
                  D QUE

     FILE 'STNGUIDE' ENTERED AT 09:48:40 ON 24 MAY 2006

     FILE 'MARPAT' ENTERED AT 09:49:12 ON 24 MAY 2006
                  D QUE L68
L69            14 SEA SSS FUL L5
                  SAVE TEMP L69 VAL348MARP/A
L70             0 SEA SUB=L69 SSS SAM L8
L71             0 SEA SUB=L69 SSS FUL L8
                  SAVE TEMP L71 VAL348MARR/A

     FILE 'STNGUIDE' ENTERED AT 09:52:14 ON 24 MAY 2006
                  D SAVED
```

D QUE STAT L69
D QUE STAT L71

FILE HOME

FILE ZCAPLUS

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FILE COVERS 1907 - 24 May 2006 VOL 144 ISS 22
FILE LAST UPDATED: 23 May 2006 (20060523/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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FILE HCAPLUS

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 19, 2006 (20060519/UP).

FILE WPIX
FILE LAST UPDATED: 18 MAY 2006 <20060518/UP>
MOST RECENT DERWENT UPDATE: 200632 <200632/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
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http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

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DICTIONARY FILE UPDATES: 23 MAY 2006 HIGHEST RN 885357-09-5

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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* *
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* *
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FILE LREGISTRY
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NEW CAS INFORMATION USE POLICIES, ENTER HELP USAGETERMS FOR DETAILS.

FILE BEILSTEIN
FILE LAST UPDATED ON MARCH 15, 2006

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,516,393 SUBSTANCES

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information by combining with PRE/FA, REA/FA or more generally
with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
between a BEILSTEIN compound and belonging reactions. For mo
detailed reaction searches BRNs can be searched as reaction

partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

```
**********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.                *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE   *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE          *
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**********************************************************************
```

NEW

*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**

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FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 May 2006 (20060518/PD)
FILE LAST UPDATED: 18 May 2006 (20060518/ED)
HIGHEST GRANTED PATENT NUMBER: US7047565
HIGHEST APPLICATION PUBLICATION NUMBER: US2006107430
CA INDEXING IS CURRENT THROUGH 18 May 2006 (20060518/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 May 2006 (20060518/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 23 May 2006 (20060523/PD)
FILE LAST UPDATED: 23 May 2006 (20060523/ED)
HIGHEST GRANTED PATENT NUMBER: US2006027591
HIGHEST APPLICATION PUBLICATION NUMBER: US2006106932
CA INDEXING IS CURRENT THROUGH 23 May 2006 (20060523/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 23 May 2006 (20060523/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006

FILE MEDLINE
FILE LAST UPDATED: 23 MAY 2006 (20060523/UP). FILE COVERS 1950 TO DATE.

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http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 17 May 2006 (20060517/ED)

FILE PASCAL
FILE LAST UPDATED: 22 MAY 2006 <20060522/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
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FILE JICST-EPLUS
FILE COVERS 1985 TO 15 MAY 2006 (20060515/ED)

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FILE EMBASE
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FILE COVERS 1978 TO 12 May 2006 (20060512/ED)

FILE DRUGU
FILE LAST UPDATED: 19 MAY 2006 <20060519/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

FILE DRUGB
>>> FILE COVERS 1964 TO 1982 - CLOSED FILE <<<

FILE VETU
FILE LAST UPDATED: 02 JAN 2002 <20020102/UP>
FILE COVERS 1983-2001

FILE VETB
FILE LAST UPDATED: 25 SEP 94 <940925/UP>
FILE COVERS 1968-1982

FILE SCISEARCH

FILE COVERS 1974 TO 18 May 2006 (20060518/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE CONF
FILE LAST UPDATED: 23 DEC 2005 <20051223/UP>
FILE COVERS 1976 TO 2005.

<<< CONF IS NO LONGER BEING UPDATED AS OF JANUARY 2006 >>>

FILE CONFSCI
FILE COVERS 1973 TO 10 Apr 2006 (20060410/ED)

CSA has resumed updates, see NEWS FILE

FILE DISSABS
FILE COVERS 1861 TO 28 APR 2006 (20060428/ED)

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 144 ISS 21 (20060519/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES (COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2006062725	23 MAR 2006
DE	102004043368	09 MAR 2006
EP	1632495	08 MAR 2006
JP	2006066839	09 MAR 2006
WO	2006042453	27 APR 2006
GB	2416167	18 JAN 2006
FR	2875804	31 MAR 2006
RU	2270725	27 FEB 2006
CA	2514373	19 FEB 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

=>